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Complete List of Authors:	Amezcua-Prieto, Carmen; University of Granada, Department of Preventive Medicine and Public Health, School of Medicine Ross, Jennifer; Centre for Trauma Sciences, Blizard Institute, Barts and the London School of Medicine and Dentistry Rogozińska, Ewelina; Queen Mary University of London, Women's Health Research Unit, Barts and the London School of Medicine and Dentistry, Queen Mary University of London; Meta-analysis Group, MRC Clinical Trials Unit, University College London, London, United Kingdom Mighiu, Patritia; Queen Mary University of London, Yvonne Carter Building, E12AB London, United Kingdom Martínez-Ruiz, Virginia; University of Granada, Preventive Medicine and Public Health Brohi, Karim; Queen Mary University of London, Centre for Trauma Sciences; Barts Health NHS Trust Bueno Cavanillas, Aurora; Universidad de Granada, Medicina Preventiva y Salud Pública Khan, Khalid; Queen Mary, University of London, Centre for Primary Care and Public Health Thangaratinam, Shakila; Birmingham Womens Hospital; Queen Mary University of London, Women's Health Research Unit, Barts and the London School of Medicine and Dentistry

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Maternal trauma due to motor vehicle crashes and pregnancy outcomes: A systematic review and meta-analysis

Amezcua-Prieto C [1,2,3],Ross J[4], Rogozińska E,[5,6]Mighiu P[5], Martínez-Ruiz V[1,2,3], Brohi K[4],Bueno-Cavanillas A[1,2,3], Khan KS[5], Thangaratinam S[5]*

[1]*Department of Preventive Medicine and Public Health. Faculty of Medicine. University of Granada. Avenida de la Investigación, 11; 18071 Granada, Spain*

[2]*CIBER de Epidemiología y Salud Pública. (CIBERESP), Granada, Spain*

[3]*Instituto de Investigación Biosanitaria ibs.GRANADA, Granada, Spain*

[4]*Centre for Trauma Sciences, Queen Mary University of London, London, United Kingdom*

[5]*Women's Health Research Unit, Barts and the London School of Medicine and Dentistry, London, United Kingdom*

[6]*Meta-analysis Group, MRC Clinical Trials Unit, University College London, London, United Kingdom*

Correspondence to:

Aurora Bueno-Cavanillas, PhD, Professor

Professor of Preventive Medicine and Public Health

Department of Preventive Medicine and Public Health, Faculty of Medicine, The University of Granada, Avenida de la Investigación, 11; 18016 Granada, Spain

CIBER de Epidemiología y Salud Pública. (CIBERESP), Granada, Spain,

Instituto de Investigación Biosanitaria ibs.GRANADA, Granada, Spain

Email: abueno@ugr.es

Abstract

Objectives

To systematically review and quantify the effect of motor vehicle crashes (MVC) in pregnancy on maternal and offspring outcomes.

Design

Systematic review and meta-analysis of observational data searched from inception until July 1, 2018.

Participants

Studies were selected if they focused on the effects of exposure MVC during pregnancy vs. non-exposure, with follow up to verify outcomes in various settings, including secondary care, collision and emergency, and inpatient care.

Data synthesis

For incidence data, we calculated a pooled estimate per 1000 women. For comparison of outcomes between women involved and those not involved in MVC, we calculated odds ratios (OR) with 95% confidence intervals (CI). Where possible, we statistically pooled the data using the random-effects model. The quality of studies used in the comparative analysis was assessed using the Newcastle-Ottawa Scale.

Results

We included 19 studies (3,222,066 women) of which the majority was carried out in high-income countries (18/19). In population-level studies of women involved in MVC, maternal death occurred in 3.6 per 1000 (95% CI 0.25 to 10.42; 3 studies, 12,000 women; Tau= 1.77), and perinatal death in 6.6 per 1000 (95% CI 3.81 to 10.12; 8 studies, 47,992 women; I^2=92.6%). The pooled incidence of complications per 1,000 women involved in MVC was labour induction (276.43), preterm delivery (191.90) and caesarean section (166.65). Compared to women not involved in MVC, those involved had increased odds of placental abruption (OR 1.43, 95% CI 1.27 to 1.63; 3 studies, 1,500,825 women) and maternal death (OR 202.27; 95% CI 110.60 to 369.95; 1 study, 1,094,559 women). Pregnant women involved in MVC using seatbelts have a lower risk of fetal death (OR 0.66 95%CI 0.36 to 1.19).

Conclusion: Pregnant women involved in MVC were at a higher risk of maternal and fetal death, and complications than those not involved.

PROSPERO registration: CRD42018100788

Key terms: Pregnancy; motor vehicle crashes; pregnancy complications

Word count: 300

Strengths and limitations of this study

- This is the first systematic review examining the link between involvement in MVC, mortality and adverse outcomes that includes evaluation of study quality assessment.
- This is the second systematic review looking at outcomes following MVC in pregnancy.
- We conducted our review using a prospectively registered protocol and reported it in accordance with the international standards.
- Outcomes variables correspond to any trimester, not to specific trimesters.
- Outcomes according to seatbelt use are scarce, since only two studies use population-level data.

Funding statement

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Competing interest's statement

There is non-financial associations that may be relevant to the submitted manuscript.

Introduction

Up to half of all women in developed countries drive motor vehicles (1) and the consequences of road traffic-related injuries involving pregnant women can be severe (2). Indeed, motor vehicle crashes (MVC) are the most common cause of non-obstetric trauma associated with fetal deaths (2.3 per 100,000 live births) (3) . The risk of adverse outcomes resulting from an MVC increases in the second trimester of pregnancy if the pregnant women were the driver (4); however, this does not appear to be the case for pregnant passengers or pedestrians (5). A maternal mortality rate of 3.5 women per 100,000 is reported following MVCs in pregnant women (6). Mechanisms of injury recorded within the pregnant population of the UK national trauma registry, the Trauma Audit and Research Network (TARN), saw an increased rate of vehicular collision in pregnant women when compared to the non-pregnant cohort (7). In 2001-2008, 2.9% of pregnant women in North Carolina were drivers in one or more crashes (8). In the USA, data from the National Automotive Sampling System (NASS/CDS) reflects that when vehicles with pregnant women are involved in an collision, 50% of those women will sustain an injury(9). There are few safety guidelines on travelling by car during pregnancy (10-12). The focus of these tends to be on questions around the use of seatbelts and the activation of airbags in the car (12).

There is a reported association between MVC and maternal mortality (13). Moreover, further associations such as the trigger for immediate delivery or being more likely to die are reported with severe blunt injury (Injury Severity Score (ISS) of 9 or above, or systolic blood pressure (SBP) <90mmHg on arrival) (14). Involvement in MVC is also associated with perinatal mortality (15), injuries to the abdominal region (16), placental abruption secondary to increased intra-abdominal pressure (17), preterm birth, and caesarean section (6). However, more data is required in relation to areas such as fetal outcomes and higher risk pregnancies, particularly regarding sociodemographic characteristics of the mother, specific trimester of pregnancy when exposed to trauma, socioeconomic country conditions, severity and type of trauma, and collision characteristics such as speed. A systematic review on trauma in pregnancy (including five studies reporting complications of involvement in MVC, and fourteen other studies on others form of trauma) showed that MVC and domestic violence were the most common causes of traumatic injury during pregnancy (4). No quality assessment of the included studies was reported in this review. Previous non-systematic reviews have published strategies used to monitor women and fetuses after a crash (18-21). However, to our knowledge there is no systematic review or meta-analysis focused on the maternal and fetal outcomes after MVC in pregnancy.

As the clinical impact on the mother and fetus after MVC has not been well documented, we conducted a systematic review of the effect on maternal and fetal outcomes of MVC in pregnant women, compared to those not involved in a collision.

Methods

We conducted a systematic review and reported it according to recommended standards (22). The review was prospectively registered with PROSPERO (no. CRD42018100788).

Literature search

The following databases were used to identify relevant literature: Medline, Embase, Web of Science, Scopus, LILACS (Latin-American and Caribbean System on Health Sciences Information), Science Citation Index, SciELO (Scientific Electronic Library Online), TRANSPORT, IRRD (International Road Research Documentation), TRANSDOC (European Conference of Ministers of Transportation databases), Cochrane Database of Systematic Reviews (CDSR), and Cochrane Central Register of Controlled Trials (CENTRAL). We also sought to identify unpublished research or research reported in the grey literature by searching a range of relevant databases, including the Inside Conferences, Systems for Information on Grey Literature (SIGLE) and Dissertation Abstracts. Furthermore, the searches of the medical database were supplemented with the Internet search using a general search engine (e.g. Google, www.google.co.uk/) and safetylit.org. Language and date restrictions were not applied to electronic searches. Relevant studies were identified using a combination of, but not limited to, the medical subject headings (MeSH) and keywords for motor vehicle collision (OR road traffic collision OR crash OR collision) and pregnancy (OR pregnant women OR gravid women OR childbearing women OR maternal).

Papers were selected if they studied the effects of exposure to trauma due to involvement in an MVC during pregnancy vs. non-exposure, with follow up to verify outcomes in various settings including secondary care, collision and emergency, and inpatient care. Observational studies (cohort studies, case-control design, non-intervention arms of randomised controlled trials) were included. Case series and case reports were excluded. Appendix 1 shows the search strategy for Medline (via Ovid) and Appendix 2 the excluded studies with reasons.

Data extraction and study quality assessment

Two reviewers (CAP & JR) independently extracted the relevant data from each full-text article and data were recorded using a standardized data extraction form. A data extraction form was piloted for each study design and amended as required. Discrepancies were resolved by consensus or by a discussion with a third senior author (ER). We extracted data on a) severe adverse maternal outcomes such as maternal death, miscarriage and preterm birth (<37/40 and <34/40); b) severe adverse fetal outcomes such as intrauterine death/stillbirth and neonatal death. Secondary outcomes were: a) individual components of maternal outcomes such as preterm labour, mode of delivery (vaginal delivery vs caesarean section), premature rupture of membranes (PROM), preterm premature rupture of membranes (PPROM), placental abruption, chorioamnionitis/sepsis and maternal admission to an intensive care unit (ICU) or high dependency unit (HDU); b) individual components of fetal outcomes: respiratory distress syndrome, neonatal ICU admission, low birth weight (LBW) and small for gestational age (SGA).

We also extracted data on 1) adverse outcomes in pregnant women involved in MVC and their offspring in subgroups according to maternal characteristics (low, high and any risk), trimester of exposure, country (low and middle income, high income), type of trauma (penetrating, blunt, burns), severity of trauma (mild, moderate, severe), seatbelt use (yes, no), study quality (low, high); 2) risk factors for pregnancy complications following MVC such as maternal characteristics (age, parity, high risk pregnancy, gestational age), type of trauma, type of motor vehicle, type of collision, collision characteristic (stationary, high or moderate speed) and seat belt use.

The quality assessment of studies was independently evaluated by two reviewers (JR and CAP) using the Newcastle-Ottawa Scale (23). This scale includes 8 items, 4 items about selection criteria of cases or cohorts in case-control or cohort designs, respectively; 2 items about comparability between groups (in both designs); and 3 items about exposure criteria in case-control designs and about outcomes in cohort designs. Any of those studies could be awarded a maximum of one star for each numbered item within the selection and exposure categories. A maximum of two stars could be given for comparability. For the incidence analysis, we considered six aspects (24): 1) representativeness of cohort; 2) design; 3) method of sampling; 4) adequacy of follow-up; 5) if the outcomes were adequately ascertained and 4) if measurement or misclassification bias were minimized. Studies without these features or with unclear reporting were classified to have a high risk of bias.

Data synthesis

We undertook random-effects meta-analysis to determine the odds ratios (OR) with 95% confidence intervals (CI) for maternal and offspring complications from MVC. We estimated heterogeneity between the included studies with Chi-Square test of Q (I2) excepting when not enough studies were in the meta-analysis (2-3), and we pooled the rates of maternal/fetal complications and reported with 95% CI. For each primary outcome, a meta-analysis was conducted for studies sufficiently homogeneous in terms of the characteristics of participants and exposure. The subgroup analysis was applied in: a) trimester of pregnancy during which the trauma occurred; b) maternal risk status (low, high, any risk); c) type of trauma; d) severity of trauma (using the ISS to categorize the severity of trauma sustained following MVC) (25); e) setting (low and middle income, high-income country); f) year of study publication: (before or after the introduction of mandatory seatbelt legislature in the country of study); and g) study quality according to the Newcastle and Ottawa Scale (23).

Results

Study selection

Out of 1,739 retrieved references, 19 studies met the eligibility criteria (Figure 1). Five of these reported data allowing us to compare pregnancy complications between pregnant women involved in MVC and those not involved in MVC (6, 26-29). The totality of the studies (n = 19) contributed to the analysis of the incidence of pregnancy complications among women involved in MVC (6, 17, 26-42).

Characteristics of included studies

The characteristics of included studies are in Table 1. Included studies were published between 1993 and 2016. Most of them were carried out in developed, high-income countries such as USA (14/18) (26, 28-31, 33-41), Sweden (1/19) (27), Kuwait (1/19) (17) and Israel (1/19) (42). The number of included pregnant women varies, ranging from 39 to 1,094,559. The data was sourced from hospital records/trauma registries (7/19) (17, 31, 32, 35, 38, 39, 42) or from population-level databases (12/19) (6, 26-30, 33, 34, 36, 37, 40, 41). The majority of studies collected information on outcomes of pregnant women involved in MVC during any trimester of pregnancy. 8 out of 19 studies reported information about the use of safety devices such as seatbelts and/or airbag (26, 29, 30, 33, 35, 37-39). Also in eight studies, the authors assessed the severity of MVC injuries with five of these using a validated tool (28, 31, 35, 38, 42) – most of them reporting ISS (28, 31, 35, 42) and one the Revised Trauma Scale (38) .

Quality assessment

60% of studies had a low risk of bias with regards to the adequacy of representativeness and random sample selection (12/19). None of the studies was prospective. The categories of follow up of more than 80% of participants, outcome ascertainment and misclassification bias showed low risk (Figure 2). The five papers included for comparison of complication rates between pregnant women exposed to MVC and those who were not exposed (assessed using the Newcastle-Ottawa Scale) showed generally high quality, with four papers scoring 9/9 (6, 26, 28, 29) . The remaining paper scored 8/9, losing one point for the comparability as it did not control for any secondary factors (27).

Incidence of complications among pregnant women involved in motor vehicle crashes

The assessment of adverse outcome incidence among women involved in MVC (using population-level data) demonstrated incidence estimations of 276.43 per 1000 for induction of labour (95%CI 262.54 to 290.54), 191.90 per 1000 for preterm delivery (95%CI 45.98 to 405.74), and 166.65 per 1000 for caesarean section (95%CI 47.34 to 339.00). The estimated incidence rates for other complications included 42.33 per 1000 for PROM, 17.08 per 1000 requiring admission to hospital, 16.14 per 1000 for placental abruption and 15.19 per 1000 for neonatal respiratory distress. A pooled incidence of maternal death was 3.60 per 1000 women (95%CI 0.25 to 10.42, 3 studies, 12,000 women, Tau=1.77). The pooled incidence of perinatal death per 1000 women was 6.60, (95% CI 3.81 to 10.12; 8 studies, 47,992 women; I^2=92.6%) (Table 2). The representation of the maternal and offspring outcomes according to trauma severity are in appendices (Appendices 3 and 4). Using data from single hospital centres, the random pooled estimation for the incidence of admission to hospital was 117.92 per 1000 women (95%CI 109.82 to 126.40) (17, 38); for maternal death was 135.05 per 1000 women (95%CI 131.37 to 138.80) and for fetal death was 5.73 per 1000 women (95% CI 3.05 to 9.77) (Appendices 5 and 6).

Pregnancy complications in women involved vs not involved in motor vehicle crashes

We observed a statistically significant link between involvement in MVC and maternal death (OR 202.3, 95%CI 110.60 to 370.00; single study) (27) (data not shown in table or graphic). Figure 3 shows pooled results from population-level data, demonstrating a positive association between MVC and placental abruption (OR 1.43 95% CI 1.27 to 1.63). Two studies contributed data used in sensitivity analyses stratifying by seatbelt use, where the pooled estimation (26, 29) of fetal death decreased with seatbelt devices (OR 0.66 95% CI 0.36 to 1.19) (Figure 4, supplementary). The review manager forest plot displays a positive but not statistically significant association between fetal death and MVC without seatbelt use (OR 5.78 95% CI 0.17 to 201.12, Tau^2 = 6.51) (Figure 5, supplementary).

Discussion

Statement of principal findings

This review estimated that for women involved in MVC, maternal death occurrence was 3.6 per 1000 and perinatal death 6.6 per 1000 women. Compared to women not involved in MVC, those involved had an increased odds of placental abruption, perinatal death, antepartum haemorrhage and maternal death. Pregnant women involved in MVC who use seatbelts have a lower risk of fetal death. The pooled incidence of complications per 1,000 women involved in MVC was, from the higher incidence to the lower, induction of labour, preterm delivery, caesarean section, premature rupture of membrane, and placental abruption (population level-data).

Strengths and weaknesses of this study

This is the second systematic review, after the one of Mendez Figueroa et al., in 2013 (4), looking at outcomes following MVC in pregnancy. We conducted our review using a prospectively registered protocol (PROSPERO) and reported it in accordance with the international standards (43). This review, to our best knowledge, is the first one examining the link between involvement in MVC, mortality and adverse outcomes that involves evaluation of study quality assessment; 14 studies looking at outcome incidence related to MVC (17, 30-42) and 5 studies comparing outcomes in pregnant women involved in MVC and those who were not (6, 26-29). We used established tools to assess outcome reporting quality for the incidence rates (44) and comparability (45). We included data from population-level and single centre studies, but the analysis and reporting of the results were independent in order to get precision and validity in the estimations. However, a couple of graphics of the maternal and offspring's outcomes incidences have been included as Appendix 3 and 4. Between August 2018 and September 2019, there have been no new studies eligible to include in the systematic review.

For the incidence analysis, we evaluated the quality of the 19 studies of this systematic review. The highest risk was in the design. None of the studies had a prospective design. The representativeness of cohort and the random method of sampling were other limitations of the quality of studies, with 7 out of 19 studies having a high risk of bias in these areas (17, 31, 32, 35, 38, 39, 42). However, the quality assessment of the five papers included for comparison of complication rates between pregnant women involved and not involved in MVC using the Newcastle-Ottawa Scale showed generally high quality, with four papers scoring 9/9 (6, 26, 28, 29).

The weaknesses of this systematic review are as follows. Firstly, outcomes were not reported by trimester, with 13 out of 19 papers focused on MVC at any trimester. Secondly, outcomes, according to seatbelt use, are scarce as only two studies using population-level data looked at safety features as a stratification factor (26, 29). Two studies with data sourced from hospital records/single-site trauma registries (38, 39) and three studies utilising population-level databases (26, 29, 30) reported some outcomes regarding seatbelt-use. Thirdly, we found a limited number of relevant studies comparing outcomes between women involved and not involved in MVC. The majority of the studies were carried out in the USA (26, 28, 29) with most recent one published in 2013 (29). Fourthly, we found heterogeneity in the included studies, seven of them have been carried out using hospital records/single-site trauma registry (17, 31, 32, 35, 38, 39, 42) and twelve using population database (6, 26-30, 33, 34, 36, 37, 40, 41). Finally, in only eight studies did authors assess severity of MVC injuries, with only five of these using a validated tool (28, 31, 35, 38, 42). This was a challenge when aiming to analyse results according to the severity of the crash.

Meaning of the study

The principle outcomes reported in the comparability studies, all of them cohort studies from population database, were perinatal death (4/5) (6, 26, 27, 29), placental abruption and any preterm delivery (3/5) (6, 28, 29), being the most strong association with MVC maternal death, but this outcome comes from a single population database study (27). The principles outcomes according to the population level in descendant order of incidence estimate per 1000 were the induction of labour, preterm delivery, caesarean section, premature rupture of membranes, and admission to hospital, placental abruption and maternal death. The pooled result using meta-analysis of proportion (random-effects model) was placental abruption (outcome reported in three studies) (6, 28, 29). In this systematic review, stratifying by seatbelt use, we appreciated a higher association of fetal death with a non-seatbelt use when pregnant women were involved in an MVC. Previous studies have shown that pregnant women wearing a seatbelt during their MVC are not at a significantly higher risk of adverse fetal outcomes than women with no MVC involvement (46), and airbags contribute to the protection of both pregnant drivers and their fetuses (47).

The results from this systematic review and meta-analysis allow us to adopt primary prevention measures, recommendations and educational interventions related to the prevention of motor vehicle crashes in pregnancy, which should be incorporated into the primary care pregnancy guidelines.

Unanswered questions and future research

The effects of MVC in pregnant women is a specific field that requires further research and an improved methodological approach to determine the risks of adverse maternal and fetal outcomes.

Additional variables such as trauma severity, the position of the women in the car, use of seatbelt, deployment or non-deployment of an airbag, severity of the crash and gestational week of pregnancy should be recorded in relation to MVC exposure in order to allow more precision when analysing outcomes. A greater number of studies in a variety of global settings would also confer more consistency in the outcomes.

Conclusions

Pregnant women involved in MVC have a higher risk of maternal and fetal death and complications than those not involved. These risks are associated with not using seatbelt devices, and complications include induction of labour, preterm delivery and caesarean section. Road traffic authorities should be conscious and strict in targeting preventive measures in pregnant women at risk of MVC.

Word count: 3,032

Author's contribution

PM conducted literature searches and screened publications jointly with JR. CAP and JR extracted the data. CAP and ER drafted the manuscript and conducted the statistical analyses. KSK and ST designed the study review. CAP is the guarantor. Authors VMR, KB, ABC, ST and KSK gave critical revision of the manuscript. All authors had full access to the data and take responsibility for the data analyses. The corresponding author attests that all listed authors meet authorship criteria.

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Data sharing Statement

No additional data available

Table 1. Characteristics of included studies

Study ID Author, year, Country	Design	Sample size	Time period	Inclusion criteria	Data source	Trimester	Seatbelt use (with data)	Assessment of trauma severity (with data)	Method of assessing trauma severity	Maternal outcomes	Offspring outcomes
Population-level data											
Azar, 2005 USA	population-based matched retrospective cohort *(incidence only)*	5936	2003-2011	Admitted to hospital following MVC while pregnant	Population-based cohort	any	no	no	N/A	Maternal death	------------
Hyde, 2003 USA	retrospective cohort *(incidence and comparison)*	322704	1992-1999	Pregnant drivers involved in MVC	Linked databases (police registry & birth/death certificates)	any	yes	yes	Study-specific definition[1]	------------	Fetal death
Kvarnstrand, 2008 Sweden	retrospective cohort *(incidence and comparison)*	1094559	1991-2001	Maternal inclusion on the accident register > 28 GW	Linked databases (police registry & birth/death certificates)	2nd	no	yes	Study specific definition[2]	Maternal death	Fetal/neonatal death
Kuo, 2007 USA	retrospective chart/database review *(incidence only)*	16982 injured 4479 (in MVC)	2002	Pregnant women hospitalized with injury (only MVC used)	Sample from population level cohort (National Inpatient Sample)	any	no	no	N/A	Delivery, hospitalization	------------
Schiff, 2005 USA	retrospective cohort *(incidence and comparison)*	17899	1989-2001	Hospitalized for MVC and with a singleton livebirth or fetal death	Linked databases (hospital discharge data & birth/death certificates)	any	no	yes	ISS	Preterm birth, PROM, C-section, placental abruption	Stillbirth LBW, SGA, Fetal distress, RDS, Meconium
Schiff, 2010 USA	retrospective cohort *(incidence only)*	3348	2002-2005	Nonrollover MVC among pregnant front seat occupants	Linked databases (hospital discharge data & birth/death certificates)	any	yes (airbag) no (seatbelt)	no	N/A	Preterm birth, placental abruption, labour induction, C-section	Stillbirth, LBW SGA, RDS Fetal distress Meconium
Vivian-Taylor, 2012 Australia	retrospective cohort *(incidence and comparison)*	604380	2000-2007	Women who gave birth exposed and not exposed to MVC	Linked databases (hospital discharge data & birth/death certificates)	2nd	no	yes	Study-specific definition[3]	Admission, placental abruption, APH,PPH, preterm birth, C-section	Perinatal death, neonatal transfer

Vladutiu, 2013 USA	retrospective cohort *(incidence and comparison)*	878546	2001-2008	Pregnant women 16-46 years, > 20GW, delivering a live/ stillbirth singleton infant	Linked databases (police registry & birth/death certificates)	2nd	yes (seatbelt) yes (airbag)	no	N/A	Placental abruption, PROM, preterm birth	Stillbirth
Weiss, 2002 USA	crash database pregnant vs. non-pregnant (NASS/CDS) *(incidence only)*	32810	1995-1999	Pregnant and non-pregnant women 15–39 years	Sample from population-level database of traffic accidents	any	yes	no	N/A	Maternal death	------------
Weiss, 2008 USA	retrospective cohort *(incidence only)*	1816	1999-2002	Injury-related emergency department visits by pregnant women (only MVC used)	Linked databases (hospital discharge data & birth/death certificates)	any	no	no	N/A	Hospital admission	------------
Whitehead, 2013* USA	PRAMS survey database *(incidence only)*	235329	2000-2005	Survey of women who recently delivered a live-born infant	Population-based cohort (PRAMS)	any	no	no	N/A	Preterm birth, UTI, PROM	------------
Wolf, 1993 USA	population-based retrospective cohort *(incidence only)*	2582	1980-1988	Pregnant women drivers involved in MVC >20GW	Linked databases (police registry & birth/death certificates)	2nd & 3rd	yes	no	N/A	Preterm birth, placental abruption, C-section	Stillbirth, LBW, RDS
Single hospital records/trauma registry											
Aboutanos, 2007 USA	retrospective chart/database review *(incidence only)*	148	2001-2005	Pregnant women presenting to ED following MVC	Single hospital records from trauma centre	any	yes (only in miscarriage)	yes	ISS	Maternal death, miscarriage	Fetal death hydrops fetalis
Baerga-Varela, 2000 USA	retrospective chart/database review *(incidence only)*	39	1986-1996	Admitted to hospital after MVC while pregnant	Single hospital records	any	no	yes	ISS	Maternal death, miscarriage	Stillbirth
Brookfield, 2013 USA	retrospective chart/database review *(incidence only)*	256	1990-2007	Pregnant women presenting to ED following MVC	Single hospital records from trauma centre	any	yes	yes	ISS and RTS	Maternal death, admission to hospital	------------

Chibber, 2015 Kuwait	**retrospective chart/database review** ***(incidence only)***	**728**	**2009-2012**	**MVC, pregnant, treated at major tertiary hospitals**	**Single hospital records**	**2^{nd}**	**no**	**no**	**N/A**	**Maternal death, placental abruption, preterm birth, uterine rupture, C-Section, admission**	**Fetal death, fetal distress**
Luley, 2013 USA	retrospective chart/database review *(incidence only)*	126	1994-2010	Pregnant women after an MVC >14/40 GA	Single hospital trauma database	2^{nd} & 3^{rd}	yes	no	N/A	Maternal death, placental abruption, C-section	Stillbirth
Miller, 2016 Israel	retrospective cohort *(incidence only)*	3794	2006-2013	Women 18-40 years, in MVC and hospitalized (only pregnant cohort used)	National trauma registry	any	no	no	ISS	Maternal death, miscarriage, placental abruption, C-section	Stillbirth
Orji, 2002 Nigeria	retrospective chart/database review *(incidence only)*	84	1980-2000	Pregnant women in MVC managed in tertiary hospitals	Single hospital records**	any	no	no	N/A	Maternal death, placental abruption, uterine rupture, C-section	Perinatal death, fetal tachycardia

*ISS: Injury Severity Score; RTS: Revised Trauma Score; ICU: Intensive Care Unit, N/A not applicable; GA: Gestational Age; LBW: Low birth weight; SGA: Small for gestational age; RDS: Respiratory distress syndrome. *National survey; **Two hospitals in same region included; [1]Possible/probable/incapacitated/fatal; [2]Fatal/major/minor/uninjured; [3]'Severe' = admission to ICU and/or blood transfusion and/or injury to abdomen/pelvis/lower back.*

Table 2. Incidence of adverse outcomes per 1,000 women involved in motor vehicle crashes – data source: population databases

Outcome	Number of studies	Number of women	Incidence estimate per 1,000 women	95% CI
Maternal				
Maternal death	3	12000	3.60	(0.25 to 10.42)
Admission to hospital	2	3838	17.08	(13.20 to 21.46)
Placenta abruption	6	36737	16.14	(7.04 to 28.78)
Preterm delivery	5	265680	191.90	(45.98 to 405.74)
Premature Rupture of Membranes	3	260310	42.33	(5.87 to 109.24)
Labour induction	2	3930	276.43	(262.54 to 290.54)
Caesarean section	5	12338	166.65	(47.34 to 339.00)
Offspring				
Fetal death	3	8210	5.97	(2.23 to 11.41)
Perinatal death	8	47992	6.60	(3.81 to 10.12)
Fetal distress	2	3930	60.09	(52.85 to 67.77)
Meconium at delivery	2	3930	52.61	(45.82 to 59.85)
Respiratory Distress Syndrom	3	6522	15.19	(5.83 to 28.68)

CI, Confidence Interval

Figures

Figure 1. The study selection process in the systematic review of outcomes on pregnant women involved in motor vehicle crashes

Figure 2. The quality assessment of the included studies

Figure 3. Comparison of outcomes between women involved and not involved in motor vehicle crashes

Figure 4. (Supplementary). Comparison of pregnancy complication between women involved and not involved in motor vehicle crashes stratified by seatbelt use

Figure 5. (Supplementary). Comparison of maternal and fetal death between women involved and not involved in motor vehicle crashes stratified by seatbelt use

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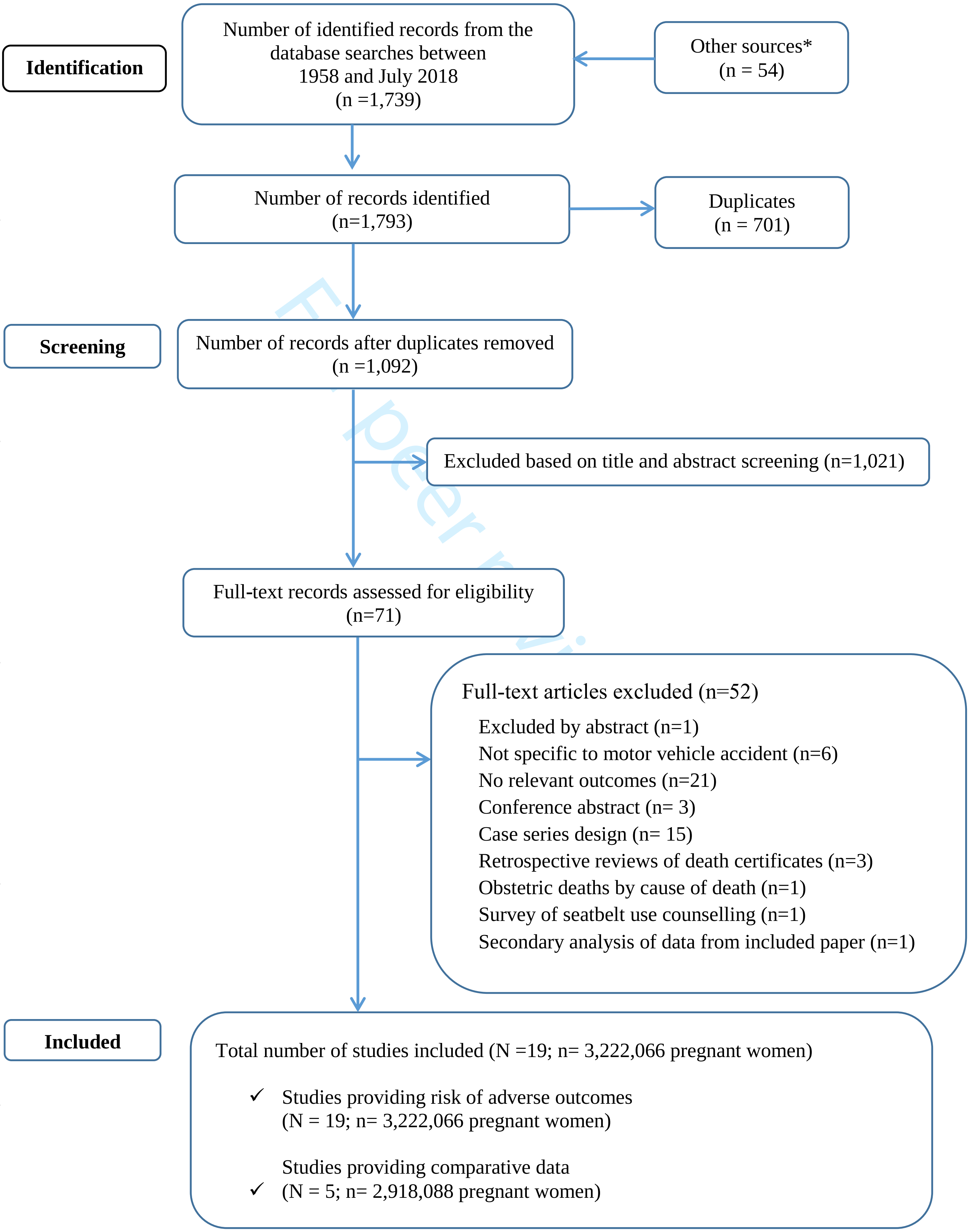
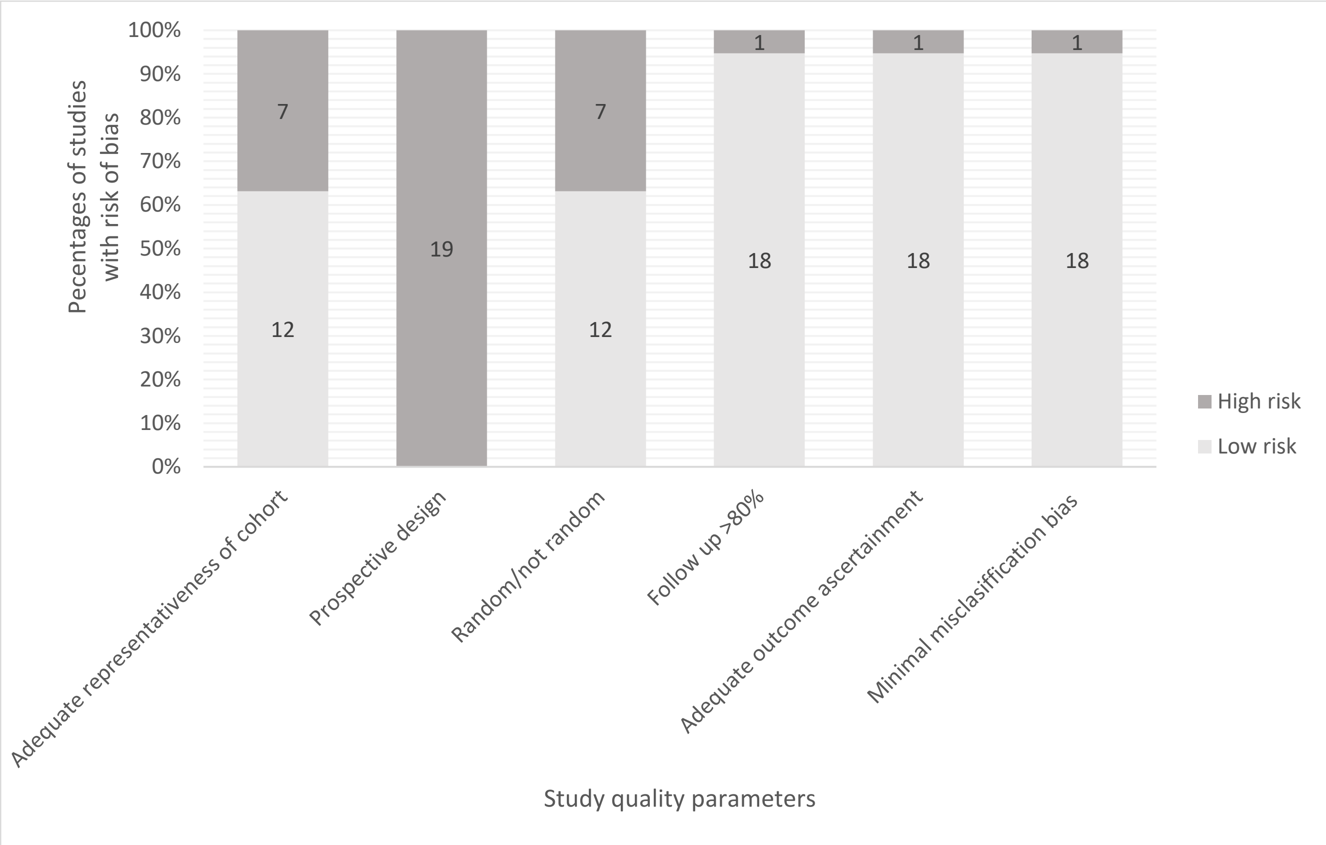
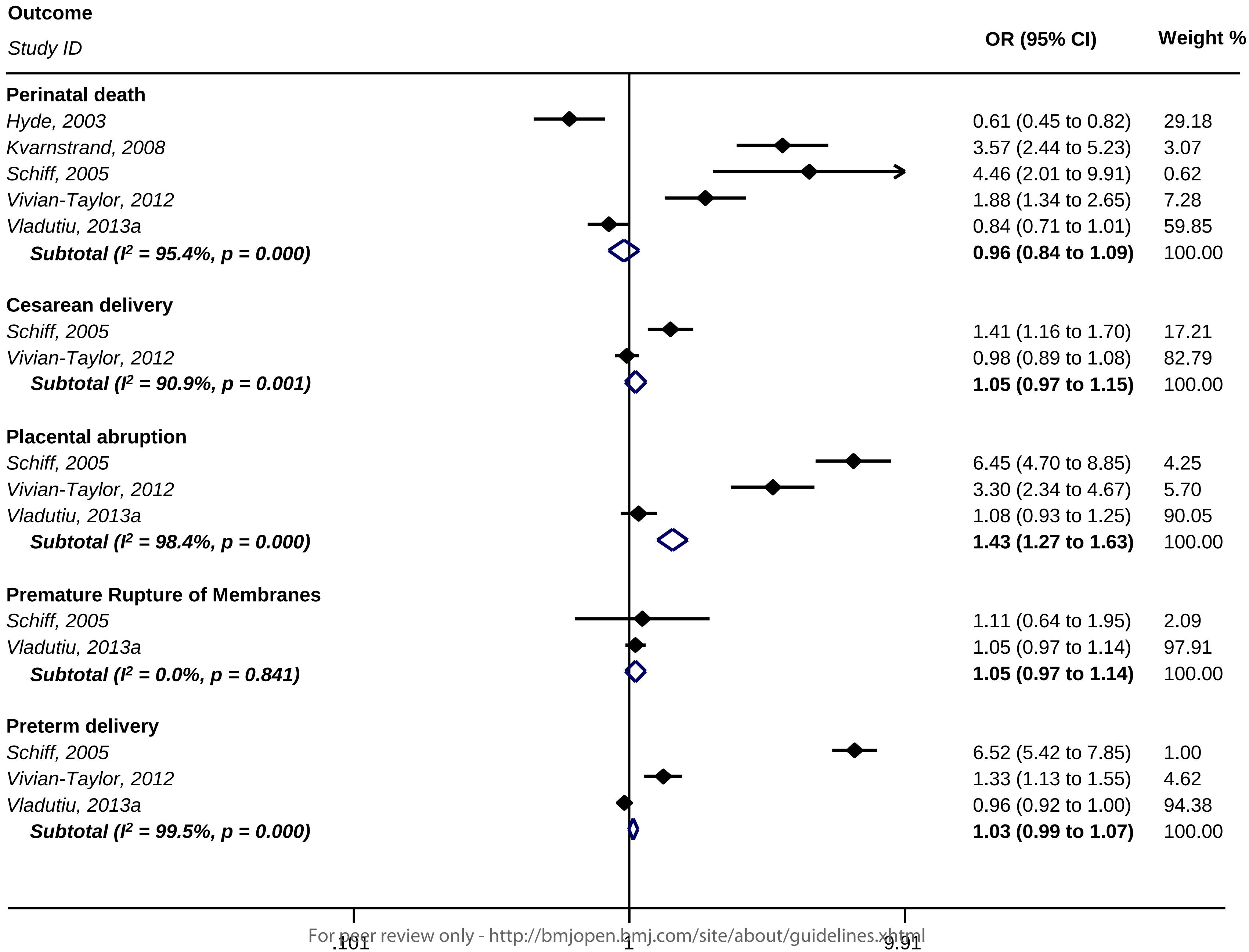
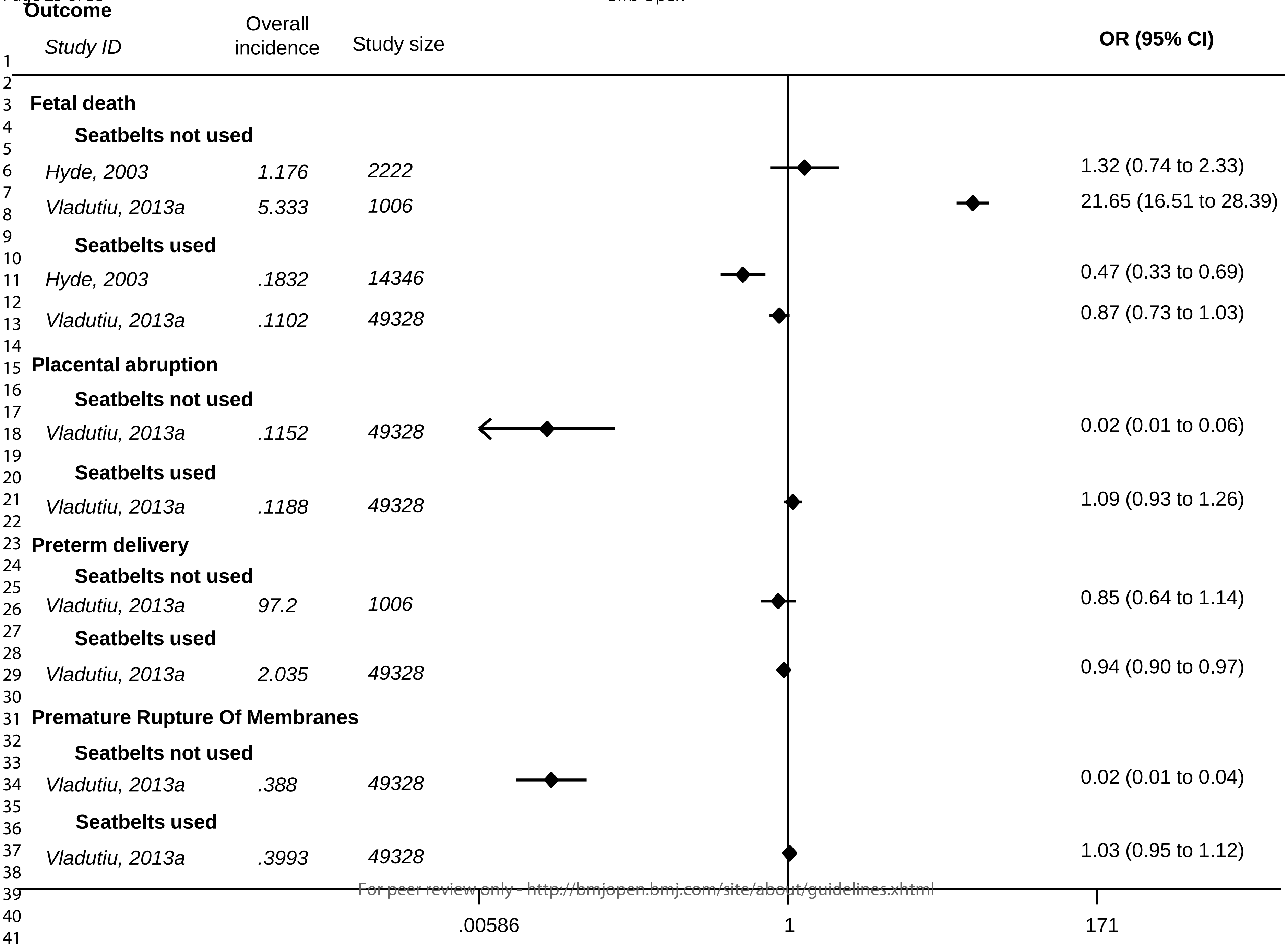


**references of relevant non-systematic reviews and Google scholar*



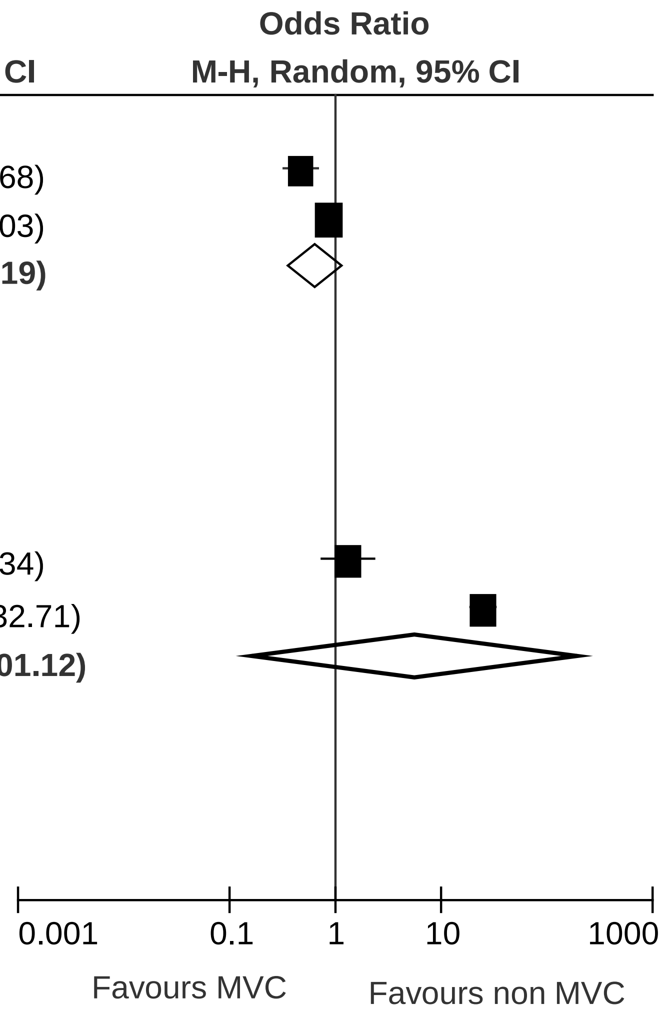
Pecentages of studies with risk of bias
100%
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
7
12
19
7
12
1
18
1
18
1
18
High risk
Low risk
Adequate representativeness of cohort
Prospective design
Random/not random
Follow up >80%
Adequate outcome ascertainment
Minimal misclasiffication bias
Study quality parameters


Outcome
Study ID
OR (95% CI)
Weight %
Perinatal death
Hyde, 2003
0.61 (0.45 to 0.82)
29.18
Kvarnstrand, 2008
3.57 (2.44 to 5.23)
3.07
Schiff, 2005
4.46 (2.01 to 9.91)
0.62
Vivian-Taylor, 2012
1.88 (1.34 to 2.65)
7.28
Vladutiu, 2013a
0.84 (0.71 to 1.01)
59.85
Subtotal (I² = 95.4%, p = 0.000)
0.96 (0.84 to 1.09)
100.00
Cesarean delivery
Schiff, 2005
1.41 (1.16 to 1.70)
17.21
Vivian-Taylor, 2012
0.98 (0.89 to 1.08)
82.79
Subtotal (I² = 90.9%, p = 0.001)
1.05 (0.97 to 1.15)
100.00
Placental abruption
Schiff, 2005
6.45 (4.70 to 8.85)
4.25
Vivian-Taylor, 2012
3.30 (2.34 to 4.67)
5.70
Vladutiu, 2013a
1.08 (0.93 to 1.25)
90.05
Subtotal (I² = 98.4%, p = 0.000)
1.43 (1.27 to 1.63)
100.00
Premature Rupture of Membranes
Schiff, 2005
1.11 (0.64 to 1.95)
2.09
Vladutiu, 2013a
1.05 (0.97 to 1.14)
97.91
Subtotal (I² = 0.0%, p = 0.841)
1.05 (0.97 to 1.14)
100.00
Preterm delivery
Schiff, 2005
6.52 (5.42 to 7.85)
1.00
Vivian-Taylor, 2012
1.33 (1.13 to 1.55)
4.62
Vladutiu, 2013a
0.96 (0.92 to 1.00)
94.38
Subtotal (I² = 99.5%, p = 0.000)
1.03 (0.99 to 1.07)
100.00
.101
1
9.91


Outcome
Study ID
Overall incidence
Study size
OR (95% CI)
Fetal death
Seatbelts not used
Hyde, 2003 1.176 2222 1.32 (0.74 to 2.33)
Vladutiu, 2013a 5.333 1006 21.65 (16.51 to 28.39)
Seatbelts used
Hyde, 2003 .1832 14346 0.47 (0.33 to 0.69)
Vladutiu, 2013a .1102 49328 0.87 (0.73 to 1.03)
Placental abruption
Seatbelts not used
Vladutiu, 2013a .1152 49328 0.02 (0.01 to 0.06)
Seatbelts used
Vladutiu, 2013a .1188 49328 1.09 (0.93 to 1.26)
Preterm delivery
Seatbelts not used
Vladutiu, 2013a 97.2 1006 0.85 (0.64 to 1.14)
Seatbelts used
Vladutiu, 2013a 2.035 49328 0.94 (0.90 to 0.97)
Premature Rupture Of Membranes
Seatbelts not used
Vladutiu, 2013a .388 49328 0.02 (0.01 to 0.04)
Seatbelts used
Vladutiu, 2013a .3993 49328 1.03 (0.95 to 1.12)
.00586
1
171

Study ID (Subgroup)	MVC Events	MVC Total	Non MVC Events	Non MVC Total	Weight	Odds Ratio M-H, Random, 95% CI
Fetal deaths (seatbelts used)						
Hyde 2003	28	7145	2600	313674	46.2%	0.47 (0.32 to 0.68)
Vladutiu 2013	133	24531	5305	848073	53.8%	0.87 (0.73 to 1.03)
Subtotal (95% CI)		**31676**		**1161747**	**100.0%**	**0.65 (0.36 to 1.19)**
Total events	**161**		**7905**			
Heterogeneity: Tau² = 0.17; Chi² = 8.58, df = 1 (P = 0.003); I² = 88%						
Test for overall effect: Z = 1.39 (P = 0.16)						
Fetal death (seatbelts not used)						
Hyde 2003	12	1099	2600	313674	49.8%	1.32 (0.75 to 2.34)
Vladutiu 2013	60	443	5305	848073	50.2%	24.89 (18.93 to 32.71)
Subtotal (95% CI)		**1542**		**1161747**	**100.0%**	**5.78 (0.17 to 201.12)**
Total events	**72**		**7905**			
Heterogeneity: Tau² = 6.51; Chi² = 126.07, df = 1 (P < 0.00001); I² = 99%						
Test for overall effect: Z = 0.97 (P = 0.33)						

Test for subgroup differences: Chi² = 1.41, df = 1 (P = 0.24), I² = 28.9%



*MVC, motor vehicle crash

Appendix 1. Search strategy for MEDLINE (via Ovid) executed from database inception up to July 2018

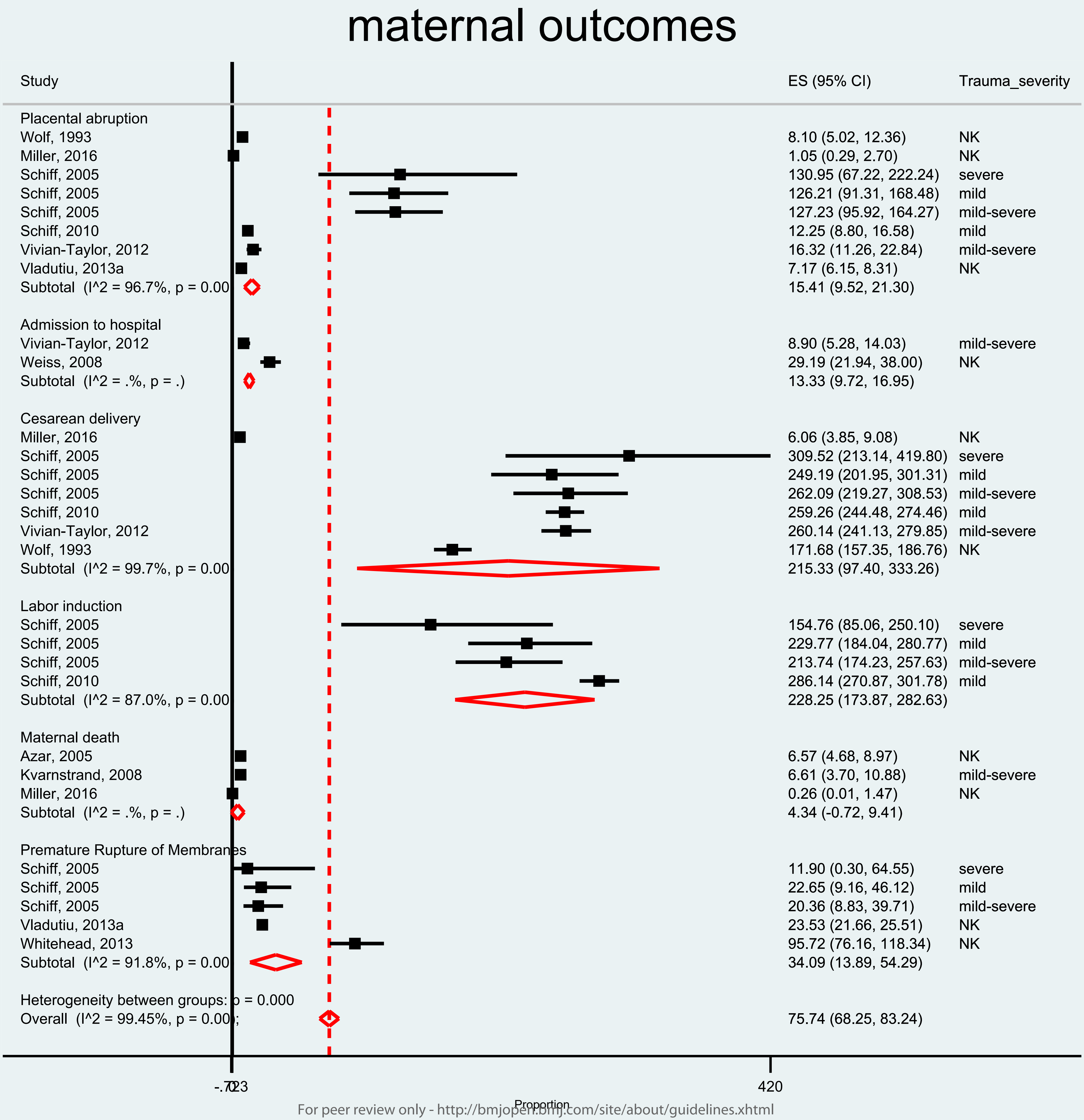
Item	Search term
1	pregnancy.af.
2	pregnan*.sh.
3	gravidity.sh.
4	gravid*.sh.
5	gestation*.sh.
6	pregnant women.sh.
7	pregnant wom#n.sh.
8	(child adj3 bearing).tw.
9	childbearing.af.
10	matern*.sh.
11	vehicle* crash*.af.
12	vehicle* accident*.af.
13	vehicle* collision*.af.
14	motor vehicle crash*.af.
15	motor vehicle accident*.af.
16	motor vehicle collision*.af.
17	motor vehicle injur*.af.
18	vehicle* injur*.af.
19	road traffic crash*.af.
20	road traffic accident*.af.
21	road traffic collision*.af.
22	road traffic injur*.af.
23	auto* crash*.af.
24	auto* accident*.af.
25	auto* collision*.af.
26	auto* injur*.af.
27	car crash*.af.
28	car accident*.af.
29	car collision*.af.
30	car injur*.af.
31	(car adj3 trauma).af.
32	(automobile adj3 trauma).af.
33	(automotive adj3 trauma).af.
34	(road traffic adj3 trauma).af.
35	(motor vehicle adj3 trauma).af.
36	1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10
37	11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34 or 35
38	36 and 37

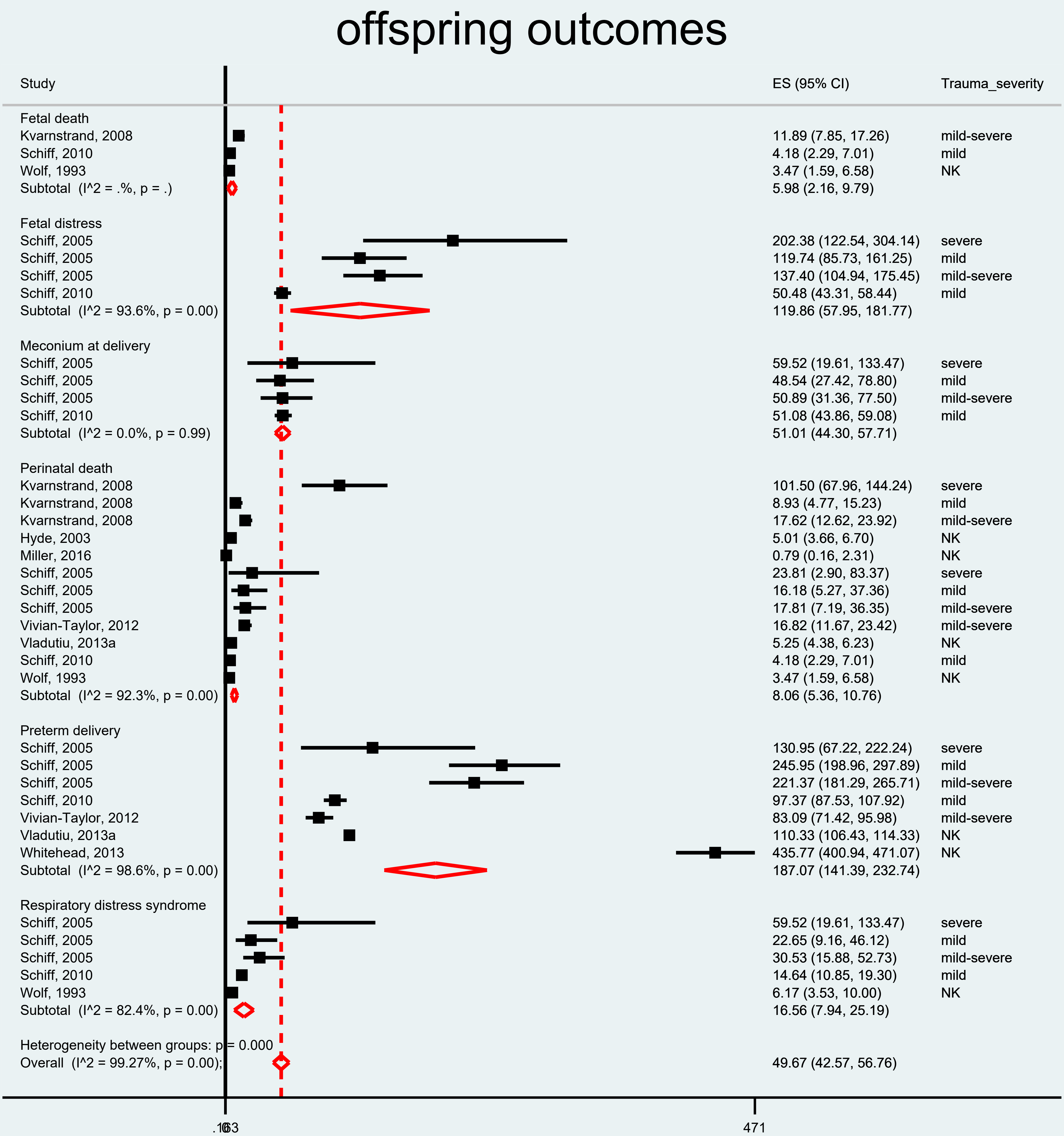
Appendix 2 List of excluded studies with reasons

Study ID	**Reason**	**Reference**
Al Mulhim, 2012	Pregnancy loss or not after trauma in Arabic pregnant women	*EMHJ. Vol. 18 No. 5 2012*
Battaloglu 2016	From a cohort of 15,140 female patients, 173 were pregnant women in the trauma registry. 55.5% of them from vehicle collision	**SR Petrone, 2017** *Injury, Int. J. Care Injured 47 (2016) 184-187*
Barre 2006	Pregnant women with abdominal trauma during pregnancy (n=65). Half of them from a traffic accident.	**SR Petrone, 2017** *La Revue Sage-Femme. Vol 5, Issue 6, 2006, 312-316*
Cannada 2010	Pregnant women with orthopaedic injuries (n=65)	**SR Petrone, 2017** *Injury, Infection, and Critical Care.2010. Vol. 69 (3)*
Chamberlain, 2011	Communication abstract. Retrospective cohort study. Identification of 272 pregnant trauma victims. 78.6% of them incurred in a MVC. No data to extract	*American Journal of Obstetrics & Gynecology Supplement to January 2011*
Cheng, 2012	Maternal complications during delivery according to uninjured, minor and severe injuries. 2,881 pregnant women (47,4%) involved in MVC	*World J Surg (2012) 36:2767–2775*
Connolly, 1997	476 maternal records of trauma cases. 54.6% were MVC. No more data available	*American Journal of Perinatology.1997.Vol. 14 (6)*
Corsi 1999	Twenty-seven traumatised pregnant women were analysed retrospectively over a period of 9 years in Sao Paulo, Brazil	**SR Petrone, 2017** *Injury, Int. J. Care Injured 30 (1999) 239-243*
Dannenberg, 1995	Homicide and other injuries as causes of maternal death between 1987 and 1991 in New York	*Am J Obstet Gynecol Vol.172 (5)*
Deshpande, 2017	Trauma impact on maternal mortality. Comparability between pregnant vs. non pregnant women	*American Journal of Obstetrics & Gynecology 2017. 590.e2*
El Kady 2004	Retrospective cohort study of women hospitalized for Trauma in California	**SR Petrone, 2017** *American Journal of Obstetrics and Gynecology (2004) 190, 1661-8*
El Kady D, 2006	Fractures injuries on maternal/neonatal outcomes in United States	**SR Méndez -Figueroa 2013** *American Journal of Obstetrics and Gynecology (2006) 195, 711–6*
Fischer 2011	Minor trauma and poor fetal outcomes in Tennessee, Memphis	**SR Petrone, 2017** *Injury, Infection, and Critical Care. 2011. Vol. 71 (1)*
Gibbins, 2017	Communication. MVC and Stillbirth. Secondary analysis of 439 stillbirth	American Journal of Obstetrics & Gynecology Supplement to January 2017
Goodwin, 1990	Case-series of trauma pregnant women between 1987 and 1988 in Los Angeles	**SR Méndez -Figueroa 2013** *Am J Obstet Gynecol. 1990 Vol. 162 (3).*

Hardt, 2013	Prenatal risk screening to identify women at increased risk for traumatic pregnancy-associated death	*Women's Health Issues 23-3 (2013) e187–e193*
Hardy, 1974	Maternal mortality ratios at large urban charity hospitals from 1941 to 1971	*Obstetric and Gynecology. 1974. Vol.43 (1)*
Harland 2014	Risks factors of maternal injuries in a population-based sample of pregnant women from Iowa	**SR Petrone, 2017** *Journal of Women's Health. 2014. Vol. 23 (12)*
Hitosugi 2006	135 traffic accidents involving Japanese pregnant women from insurance companies. The outcomes of neonates determined by their condition 1 month after birth (death/abortion/healthy)	**SR Petrone, 2017** *Forensic Science International 159 (2006) 51-54*
Ikossi, 2005	Risks factors of trauma in pregnant women from San Francisco, California	*J Am Coll Surg. Vol. 2005. 200 (1)*
Lynch, 2011	Pregnancy associated- death in Ohio: 2003-2007	American Journal of Obstetrics & Gynecology Supplement to January 2011
Manoogian, 2015	Injuries characteristics between pregnant vs non pregnant women occupants (not outcome)	*Accident Analysis and Prevention 74 (2015). 69–76*
Melamed 2012	Outcomes following blunt trauma in Pregnant women from Israel	**SR Petrone, 2017** *The Journal of Maternal-Fetal and Neonatal Medicine. 2012; 25(9): 1612–1617*
Mesdaghinia, 2012	Causes of trauma in 32 pregnant women with trauma in a Hospital in Iran	*Arch Trauma Res. 2012;1(1):23-26*
Nannini, 2008	Risks of injury in pregnant women in Massachusets	*Journal of Midwifery & Women's Health.2008. Vol.53 (1)*
Omoke, 2013	Trauma during pregnancy in a Nigerian setting	*Int J Crit Illn Inj Sci. 2013; 3(4): 269–273.*
Osei-Ampofo, 2016	A cross-sectional study with 134 pregnant women from Ghana visiting the emergency care. Leading injury MVC (23%). Not outcomes	*African Journal of Emergency Medicine (2016) 6, 87 –93*
Pak, 1998	Delivery outcomes after a blunt abdominal trauma in 85 pregnant women	*Am J Obstet Gynecol. 1998. Vol. 179 (5)*
Patteson, 2007	High risk factors involved in trauma during pregnancy. Not outcomes	*The Journal of TRAUMA Injury, Infection, and Critical Care. 2007. Vol 62 (4)*
Pearlman, 1990	Not possible to assess full text	SR Méndez -Figueroa 2013
Schiff, 1997	Seat Bealt use. Protective factor of maternal mortality after a MVC in Mexico	*WJM, 1997. Vol. 167 (1)*
Schuster, 2016	Communication abstract. Impact of blunt trauma on maternal and pregnancy outcome. MVC the most common injury mechanism (70%). Pennsylvania Trauma Systems Foundation Database (1996-2013).	*American Journal of Obstetrics & Gynecology. Supplement to January 2016*
Schuster, 2018	Pennsylvania Trauma Systems Foundation Database. ISS>9 and SBP<90mmHg are predictors for poor outcomes after trauma during pregnancy	*Trauma, 2018. Vol. 20(1) 30–37*

Sela, 2011	Treatment provided to pregnant motor vehicle accident (MVA) casualties in a mature trauma system in Israel	*Annals of Surgery, 2011.Vol.254 (2)*
Shah, 1998	Trauma in general in pregnant women	*J Trauma. 1998 Jul;45(1):83-6*
Shakerian 2015	Determining adherence to recommended imaging guidelines in pregnant women from Victoria, Australia	**SR Petrone, 2017** *J Trauma Acute Care Surg. 2015.Vol. 78 (1)*
Shiff 2002	Retrospective cohort study to assess outcomes of pregnant women hospitalized for injury in Washington State from 1989 to 1997	**SR Petrone, 2017** *J Trauma. 2002; 53: 939–945.*
Sirin, 2007	Report the prevalence of seatbelt counselling by prenatal care providers during pregnancy in USA	*Matern Child Health J (2007) 11:505–510*
Tinker 2010	Risks factors involved in injuries in pregnant women from the National Birth Defects Prevention Study, USA	**SR Petrone, 2017** *Journal of Women's Health. 2010. Vol. 19 (2)*
Van der Knoop, 2015	Effect of maternal trauma in fetal motility at term and at one year of age	*Early Human Development 91 (2015) 511–517*
Van der Knoop, 2018	Matched case-control study. Neurobehavioral outcome in 6-18 year old children after trauma in pregnancy	*European Journal of Paediatric Neurology (2018), 22(5):845-853*
Vladutiu, 2013b	Same sample Vladutiu 2013a; excluded as a secondary analysis from already included study	*Accid Anal Prev. 2013; 55: 165–171*
Wahabi, 2007	45 MVC case series pregnant women collected over a 10- year period	*Saudi Med J. 2007. Vol. 28 (9)*
Wall 2014	Pregnant trauma patiens from South Africa (mainly assaults)	**SR Petrone, 2017** *Injury, Int. J. Care Injured 45 (2014) 1220–1223*
Weiner 2016	Minor trauma during pregnancy, not associated with adverse pregnancy outcomes, Israel	**SR Petrone, 2017** *European Journal Of Obstetrics & Gynecology and Reproductive Biology 203 (2016): 78–81*
Weiss, 1999	Retrospect review of death certificates	*43rd Annual Proceedings Association for the Advancement of Automotive Medicine September 20-21, 1999. Barcelona (Sitges), Spain*
Weiss, 2001	Retrospect review of death certificates	*JAMA, 2001. Vol. 286 (15)*
Weiss, 2002a	N/A	
Zangene, 2015	102 cases of trauma in pregnancy registered in Iran from 2007 to 2010. MVC the most frequent (45%)	*Global Journal of Health Science. 2015. Vol 7 (2)*


maternal outcomes
Study
ES (95% CI)
Trauma_severity
Placental abruption
Wolf, 1993
8.10 (5.02, 12.36)
NK
Miller, 2016
1.05 (0.29, 2.70)
NK
Schiff, 2005
130.95 (67.22, 222.24)
severe
Schiff, 2005
126.21 (91.31, 168.48)
mild
Schiff, 2005
127.23 (95.92, 164.27)
mild-severe
Schiff, 2010
12.25 (8.80, 16.58)
mild
Vivian-Taylor, 2012
16.32 (11.26, 22.84)
mild-severe
Vladutiu, 2013a
7.17 (6.15, 8.31)
NK
Subtotal (I^2 = 96.7%, p = 0.00
15.41 (9.52, 21.30)
Admission to hospital
Vivian-Taylor, 2012
8.90 (5.28, 14.03)
mild-severe
Weiss, 2008
29.19 (21.94, 38.00)
NK
Subtotal (I^2 = .%, p = .)
13.33 (9.72, 16.95)
Cesarean delivery
Miller, 2016
6.06 (3.85, 9.08)
NK
Schiff, 2005
309.52 (213.14, 419.80)
severe
Schiff, 2005
249.19 (201.95, 301.31)
mild
Schiff, 2005
262.09 (219.27, 308.53)
mild-severe
Schiff, 2010
259.26 (244.48, 274.46)
mild
Vivian-Taylor, 2012
260.14 (241.13, 279.85)
mild-severe
Wolf, 1993
171.68 (157.35, 186.76)
NK
Subtotal (I^2 = 99.7%, p = 0.00
215.33 (97.40, 333.26)
Labor induction
Schiff, 2005
154.76 (85.06, 250.10)
severe
Schiff, 2005
229.77 (184.04, 280.77)
mild
Schiff, 2005
213.74 (174.23, 257.63)
mild-severe
Schiff, 2010
286.14 (270.87, 301.78)
mild
Subtotal (I^2 = 87.0%, p = 0.00
228.25 (173.87, 282.63)
Maternal death
Azar, 2005
6.57 (4.68, 8.97)
NK
Kvarnstrand, 2008
6.61 (3.70, 10.88)
mild-severe
Miller, 2016
0.26 (0.01, 1.47)
NK
Subtotal (I^2 = .%, p = .)
4.34 (-0.72, 9.41)
Premature Rupture of Membranes
Schiff, 2005
11.90 (0.30, 64.55)
severe
Schiff, 2005
22.65 (9.16, 46.12)
mild
Schiff, 2005
20.36 (8.83, 39.71)
mild-severe
Vladutiu, 2013a
23.53 (21.66, 25.51)
NK
Whitehead, 2013
95.72 (76.16, 118.34)
NK
Subtotal (I^2 = 91.8%, p = 0.00
34.09 (13.89, 54.29)
Heterogeneity between groups: p = 0.000
Overall (I^2 = 99.45%, p = 0.00);
75.74 (68.25, 83.24)
-.7023
420
Proportion


offspring outcomes
Study
ES (95% CI)
Trauma_severity
Fetal death
Kvarnstrand, 2008 11.89 (7.85, 17.26) mild-severe
Schiff, 2010 4.18 (2.29, 7.01) mild
Wolf, 1993 3.47 (1.59, 6.58) NK
Subtotal (I^2 = .%, p = .) 5.98 (2.16, 9.79)
Fetal distress
Schiff, 2005 202.38 (122.54, 304.14) severe
Schiff, 2005 119.74 (85.73, 161.25) mild
Schiff, 2005 137.40 (104.94, 175.45) mild-severe
Schiff, 2010 50.48 (43.31, 58.44) mild
Subtotal (I^2 = 93.6%, p = 0.00) 119.86 (57.95, 181.77)
Meconium at delivery
Schiff, 2005 59.52 (19.61, 133.47) severe
Schiff, 2005 48.54 (27.42, 78.80) mild
Schiff, 2005 50.89 (31.36, 77.50) mild-severe
Schiff, 2010 51.08 (43.86, 59.08) mild
Subtotal (I^2 = 0.0%, p = 0.99) 51.01 (44.30, 57.71)
Perinatal death
Kvarnstrand, 2008 101.50 (67.96, 144.24) severe
Kvarnstrand, 2008 8.93 (4.77, 15.23) mild
Kvarnstrand, 2008 17.62 (12.62, 23.92) mild-severe
Hyde, 2003 5.01 (3.66, 6.70) NK
Miller, 2016 0.79 (0.16, 2.31) NK
Schiff, 2005 23.81 (2.90, 83.37) severe
Schiff, 2005 16.18 (5.27, 37.36) mild
Schiff, 2005 17.81 (7.19, 36.35) mild-severe
Vivian-Taylor, 2012 16.82 (11.67, 23.42) mild-severe
Vladutiu, 2013a 5.25 (4.38, 6.23) NK
Schiff, 2010 4.18 (2.29, 7.01) mild
Wolf, 1993 3.47 (1.59, 6.58) NK
Subtotal (I^2 = 92.3%, p = 0.00) 8.06 (5.36, 10.76)
Preterm delivery
Schiff, 2005 130.95 (67.22, 222.24) severe
Schiff, 2005 245.95 (198.96, 297.89) mild
Schiff, 2005 221.37 (181.29, 265.71) mild-severe
Schiff, 2010 97.37 (87.53, 107.92) mild
Vivian-Taylor, 2012 83.09 (71.42, 95.98) mild-severe
Vladutiu, 2013a 110.33 (106.43, 114.33) NK
Whitehead, 2013 435.77 (400.94, 471.07) NK
Subtotal (I^2 = 98.6%, p = 0.00) 187.07 (141.39, 232.74)
Respiratory distress syndrome
Schiff, 2005 59.52 (19.61, 133.47) severe
Schiff, 2005 22.65 (9.16, 46.12) mild
Schiff, 2005 30.53 (15.88, 52.73) mild-severe
Schiff, 2010 14.64 (10.85, 19.30) mild
Wolf, 1993 6.17 (3.53, 10.00) NK
Subtotal (I^2 = 82.4%, p = 0.00) 16.56 (7.94, 25.19)
Heterogeneity between groups: p = 0.000
Overall (I^2 = 99.27%, p = 0.00); 49.67 (42.57, 56.76)
.163
471
Proportion

Appendix 5. Incidence of maternal, fetal & neonatal complications from single studies

Outcome	Total sample size	Incidence estimate per 1,000 women (95%CI)
Maternal outcomes		
Placental problems	235329	100.00 (98.79, 101.22)
Miscarriage	3794	1.85 (0.74, 3.80)
Antepartum haemorrhage	2022	47.48 (38.62, 57.67)
Postpartum haemorrhage	2022	77.65 (66.35, 90.18)
Vaginal bleeding	235329	247.00 (245.26, 248.75)
Hospital stay >=6 days	5936	117.92 (109.82, 126.40)
Maternal death or hospitalisation	32810	135.05 (131.37, 138.80)
Fetal and neonatal		
Hypoxia	582	22.34 (11.95, 37.89)
Neonatal death	2270	5.73 (3.05, 9.77)
Neonatal transfer	2022	42.53 (34.16, 52.26

Appendix 6. Incidence in non-population level data

Outcome	Study ID	Number of events	Group size	Trauma severity level
Admission to hospital	Brookfield, 2013	182	256	Not given
	Chibber, 2015	648	728	Not given
Caesarean delivery	Chibber, 2015	529	728	Not given
	Luley 2013	32	126	Not given
	Orji, 2002	2	84	Not given
Fetal death	Aboutanos, 2007	1	148	Not given
	Chibber, 2015	78	728	Not given
Fetal distress	Chibber, 2015	412	728	Not given
Fetal tachycardia	Orji, 2002	10	84	Not given
Hydrops fetalis	Aboutanos, 2007	1	148	Not given
Maternal death	Aboutanos, 2007	0	148	Not given
	Baerga-Varela, 2000	1	39	Severe
	Brookfield, 2013	7	256	Not given
	Chibber, 2015	100	728	Not given
Maternal death	Orji, 2002	2	84	Not given
Miscarriage	Aboutanos, 2007	5	148	Not given
	Baerga-Varela, 2000	7	39	Mild to severe
Perinatal death	Baerga-Varela, 2000	23	39	Mild to severe
	Luley 2013	6	126	Not given
	Orji, 2002	3	84	Not given
Placental abruption	Chibber, 2015	428	728	Not given
	Luley 2013	7	126	Not given
	Orji, 2002	1	84	Not given
Preterm delivery	Chibber, 2015	97	728	Not given
Uterine rupture	Chibber, 2015	12	728	Not given
	Orji, 2002	1	84	Not given

PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	2-3
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	4
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	5
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	5
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	5-7
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	5
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	Appendix 1
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	5
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	6
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	5-7
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	8
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	8
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	8

PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	8
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	8
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	9
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	9
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	-
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	9
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	10
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	9
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	10
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	11
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	11
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	13
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	3

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Complete List of Authors:	Amezcua-Prieto, Carmen; University of Granada, Department of Preventive Medicine and Public Health, School of Medicine Ross, Jennifer; Centre for Trauma Sciences, Blizard Institute, Barts and the London School of Medicine and Dentistry Rogozińska, Ewelina; Queen Mary University of London, Women's Health Research Unit, Barts and the London School of Medicine and Dentistry, Queen Mary University of London; Meta-analysis Group, MRC Clinical Trials Unit, University College London, London, United Kingdom Mighiu, Patritia; Queen Mary University of London, Yvonne Carter Building, E12AB London, United Kingdom Martínez-Ruiz, Virginia; University of Granada, Preventive Medicine and Public Health Brohi, Karim; Queen Mary University of London, Centre for Trauma Sciences; Barts Health NHS Trust Bueno Cavanillas, Aurora; Universidad de Granada, Medicina Preventiva y Salud Pública Khan , Khalid; Women's Health Research Unit; University of Granada, Preventive Medicine and Public Health Thangaratinam, Shakila; Birmingham Womens Hospital; Queen Mary University of London, Women's Health Research Unit, Barts and the London School of Medicine and Dentistry
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Maternal trauma due to motor vehicle crashes and pregnancy outcomes: A systematic review and meta-analysis

Amezcua-Prieto C [1,2,3], Ross J[4], Rogozińska E,[5,6]Mighiu P[5], Martínez-Ruiz V[1,2,3], Brohi K[4],Bueno-Cavanillas A[1,2,3], Khan KS[1,5], Thangaratinam S[5]*

[1]*Department of Preventive Medicine and Public Health. Faculty of Medicine. University of Granada. Avenida de la Investigación, 11; 18071 Granada, Spain*
[2]*CIBER de Epidemiología y Salud Pública. (CIBERESP), Granada, Spain*
[3]*Instituto de Investigación Biosanitaria ibs.GRANADA, Granada, Spain*
[4]*Centre for Trauma Sciences, Queen Mary University of London, London, United Kingdom*
[5]*Women's Health Research Unit, Barts and the London School of Medicine and Dentistry, London, United Kingdom*
[6]*Meta-analysis Group, MRC Clinical Trials Unit, University College London, London, United Kingdom*

Correspondence to:
Aurora Bueno-Cavanillas, PhD, Professor
Professor of Preventive Medicine and Public Health
Department of Preventive Medicine and Public Health, Faculty of Medicine, The University of Granada, Avenida de la Investigación, 11; 18016 Granada, Spain
CIBER de Epidemiología y Salud Pública. (CIBERESP), Granada, Spain,
Instituto de Investigación Biosanitaria ibs.GRANADA, Granada, Spain
Email: abueno@ugr.es

Abstract

Objectives

To systematically review and quantify the effect of motor vehicle crashes (MVC) in pregnancy on maternal and offspring outcomes.

Design

Systematic review and meta-analysis of observational data searched from inception until July 1, 2018. Searching was from June to August 2018 in Medline, Embase, Web of Science, Scopus, LILACS SciELO, TRANSPORT, IRRD, TRANSDOC, CDSR, and Cochrane Central Register CENTRAL.

Participants

Studies were selected if they focused on the effects of exposure MVC during pregnancy vs. non-exposure, with follow up to verify outcomes in various settings, including secondary care, collision and emergency, and inpatient care.

Data synthesis

For incidence data, we calculated a pooled estimate per 1,000 women. For comparison of outcomes between women involved and those not involved in MVC, we calculated odds ratios with 95% confidence intervals. Where possible, we statistically pooled the data using the random-effects model. The quality of studies used in the comparative analysis was assessed with Newcastle-Ottawa Scale.

Results

We included 19 studies (3,222,066 women) of which the majority was carried out in high-income countries (18/19). In population-level studies of women involved in MVC, maternal death occurred in 3.6 per 1,000 (95% CI 0.25 to 10.42; 3 studies, 12,000 women; Tau= 1.77), and fetal death or stillbirth in 6.6 per 1,000 (95% CI 3.81 to 10.12; 8 studies, 47,992 women; I^2=92.6%). Pooled incidence of complications per 1,000 women involved in MVC was labour induction (276.43), preterm delivery (191.90) and caesarean section (166.65). Compared to women not involved in MVC, those involved had increased odds of placental abruption (OR 1.43, 95% CI 1.27 to 1.63; 3 studies, 1,500,825 women) and maternal death (OR 202.27; 95% CI 110.60 to 369.95; 1 study, 1,094,559 women).

Conclusion: Pregnant women involved in MVC were at higher risk of maternal death and complications than those not involved.

PROSPERO registration: CRD42018100788

Key terms: Pregnancy; motor vehicle crashes; pregnancy complications

Word count: 300

Strengths and limitations of this study

- This is the first systematic review examining the link between involvement in MVC, mortality and adverse outcomes that includes evaluation of study quality assessment.
- This is the second systematic review looking at outcomes following MVC in pregnancy.
- We conducted our review using a prospectively registered protocol and reported it in accordance with the international standards.
- Outcomes variables correspond to any trimester, not to specific trimesters.
- Outcomes according to seatbelt use are scarce, since only two studies use population-level data.

Funding statement

This research received no specific grant from any funding agency in the public, commercial or not-for-profit sectors.

Competing interest's statement

There are non-financial associations that may be relevant to the submitted manuscript.

Introduction

Up to half of all women in developed countries drive motor vehicles (1) and the consequences of road traffic-related injuries involving pregnant women can be severe (2). Indeed, motor vehicle crashes (MVC) are the most common cause of non-obstetric trauma associated with fetal deaths (2.3 per 100,000 live births) (3) . The risk of adverse outcomes resulting from an MVC increases in the second trimester of pregnancy if the pregnant women were the driver (4); however, this does not appear to be the case for pregnant passengers or pedestrians (5). A maternal mortality rate of 3.5 women per 100,000 is reported following MVCs in pregnant women (6). Mechanisms of injury recorded within the pregnant population of the UK national trauma registry, the Trauma Audit and Research Network (TARN), saw an increased rate of vehicular collision in pregnant women when compared to the non-pregnant cohort (7). In 2001-2008, 2.9% of pregnant women in North Carolina were drivers in one or more crashes (8). In the USA, data from the National Automotive Sampling System (NASS/CDS) reflects that when vehicles with pregnant women are involved in collision, 50% of those women will sustain an injury(9). There are few safety guidelines on travelling by car during pregnancy (10-12). The focus of these tends to be on questions around the use of seatbelts and the activation of airbags in the car (12).

There is a reported association between MVC and maternal mortality (13). Moreover, further associations such as the trigger for immediate delivery or being more likely to die are reported with severe blunt injury (Injury Severity Score (ISS) of 9 or above, or systolic blood pressure (SBP) <90mmHg on arrival) (14). Involvement in MVC is also associated with perinatal mortality (15), injuries to the abdominal region (16), placental abruption secondary to increased intra-abdominal pressure (17), preterm birth, and caesarean section (6). However, more data are required in relation to areas such as fetal outcomes and higher risk pregnancies, particularly regarding sociodemographic characteristics of the mother, specific trimester of pregnancy when exposed to trauma, socioeconomic country conditions, severity and type of trauma, and collision characteristics such as speed. A systematic review on trauma in pregnancy (including five studies reporting complications of involvement in MVC, and fourteen other studies on others form of trauma) showed that MVC and domestic violence were the most common causes of traumatic injury during pregnancy (4). No quality assessment of the included studies was reported in this review. Previous non-systematic reviews have published strategies used to monitor women and fetuses after a crash (18-21). However, to our knowledge there is no systematic review or meta-analysis focused on the maternal and fetal outcomes after MVC in pregnancy.

Review objectives

As the clinical impact on the mother and fetus after MVC has not been well documented, we conducted a systematic review of the effect on maternal and fetal outcomes of MVC in pregnant women, compared to those not involved in a collision.

Methods

We conducted a systematic review and reported it according to recommended standards (22). The review was prospectively registered with PROSPERO (no. CRD42018100788).

Literature search

Searching was from June to August 2018. The following databases were used to identify relevant literature: Medline, Embase, Web of Science, Scopus, LILACS (Latin-American and Caribbean System on Health Sciences Information), Science Citation Index, SciELO (Scientific Electronic Library Online), TRANSPORT, IRRD (International Road Research Documentation), TRANSDOC (European Conference of Ministers of Transportation databases), Cochrane Database of Systematic Reviews (CDSR), and Cochrane Central Register of Controlled Trials (CENTRAL). We also sought to identify unpublished research or research reported in the grey literature by searching a range of relevant databases, including the Inside Conferences, Systems for Information on Grey Literature (SIGLE) and Dissertation Abstracts. Furthermore, the searches of the medical database were supplemented with the Internet search using a general search engine (e.g. Google, www.google.co.uk/) and safetylit.org. Language and date restrictions were not applied to electronic searches. Relevant studies were identified using a combination of, but not limited to, the medical subject headings (MeSH) and keywords for “motor vehicle collision” (OR road traffic collision OR crash OR collision) and “pregnancy” (OR pregnant women OR gravid women OR childbearing women OR maternal).

Review inclusion criteria

Papers were selected if they studied the effects of exposure to trauma due to involvement in an MVC during pregnancy vs. non-exposure, with follow up to verify outcomes in various settings including secondary care, collision and emergency, and inpatient care. Observational studies (cohort studies, case-control design, non-intervention arms of randomised controlled trials) were included. Case series and case reports were excluded. Appendix 1 shows the search strategy for Medline (via Ovid) and Appendix 2 the excluded studies with reasons.

Data extraction and study quality assessment

A double screening of papers was carried out. Two reviewers (CAP & JR) independently extracted the relevant data from each full-text article and data were recorded using a standardized data extraction form. A data extraction form was piloted for each study design and amended as required. Discrepancies were resolved by consensus or by a discussion with a third senior author (ER). We extracted data on a) severe adverse maternal outcomes such as maternal death, miscarriage and preterm birth (<37/40 and <34/40); b) severe adverse fetal outcomes such as intrauterine death/stillbirth and neonatal death. Secondary outcomes were: a) individual components of maternal outcomes such as preterm labour, mode of delivery (vaginal delivery vs caesarean section), premature rupture of membranes (PROM), preterm premature rupture of membranes (PPROM), placental abruption, chorioamnionitis/sepsis and maternal admission to an intensive care unit (ICU) or high dependency unit (HDU); b) individual components of fetal outcomes: respiratory distress syndrome, neonatal ICU admission, low birth weight (LBW) and small for gestational age (SGA).

We also extracted data on 1) adverse outcomes in pregnant women involved in MVC and their offspring in subgroups according to maternal characteristics (low, high and any risk), trimester of exposure, country (low and middle income, high income), type of trauma (penetrating, blunt, burns), severity of trauma (mild, moderate, severe), seatbelt use (yes, no), study quality (low, high); 2) risk factors for pregnancy complications following MVC such as maternal characteristics (age, parity, high risk pregnancy, gestational age), type of trauma, type of motor vehicle, type of collision, collision characteristic (stationary, high or moderate speed) and seat belt use.

The quality assessment of studies was independently evaluated by two reviewers (JR and CAP) using the Newcastle-Ottawa Scale (23). This scale includes 8 items, 4 items about selection criteria of cases or cohorts in case-control or cohort designs, respectively; 2 items about comparability between groups (in both designs); and 3 items about exposure criteria in case-control designs and about outcomes in cohort designs. Any of those studies could be awarded a maximum of one star for each numbered item within the selection and exposure categories. A maximum of two stars could be given for comparability. For the incidence analysis, we considered six aspects (24): 1) representativeness of cohort; 2) design; 3) method of sampling; 4) adequacy of follow-up; 5) if the outcomes were adequately ascertained and 4) if measurement or misclassification bias were minimized. Studies without these features or with unclear reporting were classified to have a high risk of bias.

Patient and Public Involvement

"No patient involved"

Data synthesis

We undertook random-effects meta-analysis to determine the odds ratios (OR) with 95% confidence intervals (CI) for maternal and offspring complications from MVC. We estimated heterogeneity between the included studies with Chi-Square test of Q (I2) excepting when not enough studies were in the meta-analysis (2-3), and we pooled the rates of maternal/fetal complications and reported with 95% CI. For each primary outcome, a meta-analysis was conducted for studies sufficiently homogeneous in terms of the characteristics of participants and exposure. The subgroup analysis was applied in: a) trimester of pregnancy during which the trauma occurred; b) maternal risk status (low, high, any risk); c) type of trauma; d) severity of trauma (using the ISS to categorize the severity of trauma sustained following MVC) (25); e) setting (low and middle income, high-income country); f) year of study publication: (before or after the introduction of mandatory seatbelt legislature in the country of study); and g) study quality according to the Newcastle and Ottawa Scale (23).

Results

Study selection

Out of 1,739 retrieved references, 19 studies met the eligibility criteria (Figure 1). Five of these reported data allowing us to compare pregnancy complications between pregnant women involved in MVC and those not involved in MVC (6, 26-29). The totality of the studies (n = 19) contributed to the analysis of the incidence of pregnancy complications among women involved in MVC (6, 17, 26-42).

Characteristics of included studies

The characteristics of included studies are in Table 1. Included studies were published between 1993 and 2016. Most of them were carried out in developed, high-income countries such as USA (14/18) (26, 28-31, 33-41), Sweden (1/19) (27), Kuwait (1/19) (17) and Israel (1/19) (42). The number of included pregnant women varies, ranging from 39 to 1,094,559. The data was sourced from hospital records/trauma registries (7/19) (17, 31, 32, 35, 38, 39, 42) or from population-level databases (12/19) (6, 26-30, 33, 34, 36, 37, 40, 41). The majority of studies collected information on outcomes of pregnant women involved in MVC during any trimester of pregnancy. 8 out of 19 studies reported information about the use of safety devices such as seatbelts and/or airbag (26, 29, 30, 33, 35, 37-39). Also in eight studies, the authors assessed the severity of MVC injuries with five of these using a validated tool (28, 31, 35, 38, 42) – most of them reporting ISS (28, 31, 35, 42) and one the Revised Trauma Scale (38) .

Quality assessment

60% of studies had a low risk of bias with regards to the adequacy of representativeness and random sample selection (12/19). None of the studies was prospective. The categories of follow up of more than 80% of participants, outcome ascertainment and misclassification bias showed low risk (Figure 2). The five papers included for comparison of complication rates between pregnant women exposed to MVC and those who were not exposed (assessed using the Newcastle-Ottawa Scale) showed generally high quality, with four papers scoring 9/9 (6, 26, 28, 29). The remaining paper scored 8/9, losing one point for the comparability as it did not control for any secondary factors (27).

Incidence of complications among pregnant women involved in motor vehicle crashes

The assessment of adverse outcome incidence among women involved in MVC (using population-level data) demonstrated incidence estimations of 276.43 per 1000 for induction of labour (95% CI 262.54 to 290.54), 191.90 per 1000 for preterm delivery (95% CI 45.98 to 405.74), and 166.65 per 1000 for caesarean section (95% CI 47.34 to 339.00). The estimated incidence rates for other complications included 42.33 per 1000 for PROM, 17.08 per 1000 requiring admission to hospital, 16.14 per 1000 for placental abruption and 15.19 per 1000 for neonatal respiratory distress. A pooled incidence of maternal death was 3.60 per 1000 women (95% CI 0.25 to 10.42, 3 studies, 12,000 women, Tau=1.77). The pooled incidence of perinatal death (fetal death or stillbirth) per 1000 women was 6.60, (95% CI 3.81 to 10.12; 8 studies, 47,992 women; I^2=92.6%) (Table 2). The representation of the maternal and offspring outcomes according to trauma severity are in appendices (Appendices 3 and 4). Using data from single hospital centres, the random pooled estimation for the incidence of admission to hospital was 117.92 per 1000 women (95% CI 109.82 to 126.40) (17, 38); for maternal death was 135.05 per 1000 women (95% CI 131.37 to 138.80) and for fetal death was 5.73 per 1000 women (95% CI 3.05 to 9.77) (Appendices 5 and 6).

Pregnancy complications in women involved vs not involved in motor vehicle crashes

We observed a statistically significant link between involvement in MVC and maternal death (OR 202.3, 95% CI 110.60 to 370.00; single study) (27) (data not shown in table or graphic). Figure 3 shows pooled results from population-level data, demonstrating a positive association between MVC and placental abruption (OR 1.43 95% CI 1.27 to 1.63). Two studies contributed data used in sensitivity analyses stratifying by seatbelt use, where the pooled estimation (26, 29) of fetal death decreased with seatbelt devices, but the association was not statistically significant (OR 0.66 95% CI 0.36 to 1.19) (Figure 1, supplementary). The review manager forest plot displays a positive but not statistically significant association between fetal death and MVC without seatbelt use (OR 5.78 95% CI 0.17 to 201.12, $Tau^2 = 6.51$) (Figure 2, supplementary).

Discussion

Statement of principal findings

This review estimated that for women involved in MVC, maternal death occurrence was 3.6 per 1000 and perinatal death 6.6 per 1000 women. Compared to women not involved in MVC, those involved had an increased odds of placental abruption, antepartum haemorrhage and maternal death. The pooled incidence of complications per 1,000 women involved in MVC was, from the higher incidence to the lower, induction of labour, preterm delivery, caesarean section, premature rupture of membrane, and placental abruption (population level-data).

Strengths and weaknesses of this study

This is the second systematic review, after the one of Mendez Figueroa et al., in 2013 (4), looking at outcomes following MVC in pregnancy. We conducted our review using a prospectively registered protocol (PROSPERO) and reported it in accordance with the international standards (43). This review, to our best knowledge, is the first one examining the link between involvement in MVC, mortality and adverse outcomes that involves evaluation of study quality assessment; 14 studies looking at outcome incidence related to MVC (17, 30-42) and 5 studies comparing outcomes in pregnant women involved in MVC and those who were not (6, 26-29). We used established tools to assess outcome reporting quality for the incidence rates (44) and comparability (45). We included data from population-level and single centre studies, but the analysis and reporting of the results were independent in order to get precision and validity in the estimations. However, a couple of graphics of the maternal and offspring's outcomes incidences have been included as Appendix 3 and 4. Between August 2018 and March 2020, there have been no new studies eligible to include in the systematic review.

For the incidence analysis, we evaluated the quality of the 19 studies of this systematic review. The highest risk was in the design. None of the studies had a prospective design. The representativeness of cohort and the random method of sampling were other limitations of the quality of studies, with 7 out of 19 studies having a high risk of bias in these areas (17, 31, 32, 35, 38, 39, 42). However, the quality assessment of the five papers included for comparison of complication rates between pregnant women involved and not involved in MVC using the Newcastle-Ottawa Scale showed generally high quality, with four papers scoring 9/9 (6, 26, 28, 29).

The weaknesses of this systematic review are as follows. Firstly, outcomes were not reported by trimester, with 13 out of 19 papers focused on MVC at any trimester. Secondly, outcomes, according to seatbelt use, are scarce as only two studies using population-level data looked at safety features as a stratification factor (26, 29). Two studies with data sourced from hospital records/single-site trauma registries (38, 39) and three studies utilising population-level databases (26, 29, 30) reported some outcomes regarding seatbelt-use. Thirdly, we found a limited number of relevant studies comparing outcomes between women involved and not involved in MVC. The majority of the studies were carried out in the USA (26, 28, 29) with most recent one published in 2013 (29). Fourthly, the included studies differed in study design with seven of them using hospital records/single-site trauma registry (17, 31, 32, 35, 38, 39, 42) and twelve population database (6, 26-30, 33, 34, 36, 37, 40, 41). Despite analysing the data within the respective study designs and incorporation of anticipated variation into the statistical model (random-effects) (46), we encountered substantial statistical heterogeneity in the pooled estimates that could not be formally explored due to a limited number of studies and poor reporting of important factors such as trauma severity. As a fifth point, these data apply to developed countries - only one of the papers included data from an underdeveloped country, perhaps influencing the outcomes that might otherwise be seen in the developed world. Finally, in only eight studies did authors assess severity of MVC injuries, with only five of these using a validated tool (28, 31, 35, 38, 42). This was a challenge when aiming to analyse results according to the severity of the crash.

Meaning of the study

The strongest association was found between placental abruption (6, 28, 29) and MVC. Maternal death was associated with involvement in MVC but this finding needs to be treated with caution as the data come from a single study (27). The outcomes in descending order of incidence estimate per 1000 (population-level data) were the induction of labour, preterm delivery, caesarean section, premature rupture of membranes, and admission to hospital, placental abruption and maternal death. In the analyses stratified by use of seatbelt, we observed an association of fetal death with lack of seatbelt use by pregnant women involved in an MVC. However, this finding was not statistically significant and informed by a limited number of studies. Previous studies have shown that pregnant women wearing seatbelt during the MVC did not experience a significantly higher risk of adverse fetal outcomes than women who were not involved in MVC (47) Furthermore, airbags seem to be contributing to the protection of both pregnant drivers and their fetuses (48).

The results of this systematic review provide evidence informing primary prevention measures, recommendations and educational interventions for pregnant women in the context of MVC that should be incorporated into the primary care guidelines.

Unanswered questions and future research

The effects of MVC in pregnant women is a specific field that requires further research and an improved methodological approach to determine the risks of adverse maternal and fetal outcomes.

Additional variables such as trauma severity, the position of the women in the car, use of seatbelt, deployment or non-deployment of an airbag, severity of the crash and gestational week of pregnancy should be recorded in relation to MVC exposure in order to allow more precision when analysing outcomes. A greater number of well-designed studies in a variety of global settings would strengthen current evidence-base.

Conclusions

Pregnant women involved in MVC seem to be at increased risk of maternal death and complications, especially placental abruption, than those not involved in MVC. The risk of complications such as preterm delivery, premature rupture of membranes and caesarean section were also increased. However, these findings need to be treated with caution due to considerable between study differences. Road traffic authorities should be conscious and strict in targeting preventive measures aimed at pregnant users of motor vehicles due to risk associated with potential involvement in MVC.

Word count: 3,137

Author's contribution

PM conducted literature searches and screened publications jointly with JR. CAP and JR extracted the data. CAP and ER drafted the manuscript and conducted the statistical analyses. KSK and ST designed the study review. CAP is the guarantor. Authors VMR, KB, ABC, ST and KSK gave critical revision of the manuscript. All authors had full access to the data and take responsibility for the data analyses.

The corresponding author attests that all listed authors meet authorship criteria.

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Data sharing Statement

Data have been extracted for original papers. Dataset generated has been used for the meta-analyses.

Table 1. Characteristics of included studies

Study ID Author, year, Country	Design	Sample size	Time period	Inclusion criteria	Data source	Trimester	Seatbelt use (with data)	Assessment of trauma severity (with data)	Method of assessing trauma severity	Maternal outcomes	Offspring outcomes
Population-level data											
Azar, 2005 USA	population-based matched retrospective cohort *(incidence only)*	5936	2003-2011	Admitted to hospital following MVC while pregnant	Population-based cohort	any	no	no	N/A	Maternal death	------------
Hyde, 2003 USA	retrospective cohort *(incidence and comparison)*	322704	1992-1999	Pregnant drivers involved in MVC	Linked databases (police registry & birth/death certificates)	any	yes	yes	Study-specific definition[1]	------------	Fetal death
Kvarnstrand, 2008 Sweden	retrospective cohort *(incidence and comparison)*	1094559	1991-2001	Maternal inclusion on the accident register > 28 GW	Linked databases (police registry & birth/death certificates)	2^{nd}	no	yes	Study specific definition[2]	Maternal death	Fetal/neonatal death
Kuo, 2007 USA	retrospective chart/database review *(incidence only)*	16982 injuries 4479 (in MVC)	2002	Pregnant women hospitalized with injury (only MVC used)	Sample from population level cohort (National Inpatient Sample)	any	no	no	N/A	Delivery, hospitalization	------------
Schiff, 2005 USA	retrospective cohort *(incidence and comparison)*	17899	1989-2001	Hospitalized for MVC and with a singleton livebirth or fetal death	Linked databases (hospital discharge data & birth/death certificates)	any	no	yes	ISS	Preterm birth, PROM, C-section, placental abruption	Stillbirth LBW, SGA, Fetal distress, RDS, Meconium
Schiff, 2010 USA	retrospective cohort *(incidence only)*	3348	2002-2005	Nonrollover MVC among pregnant front seat occupants	Linked databases (hospital discharge data & birth/death certificates)	any	yes (airbag) no (seatbelt)	no	N/A	Preterm birth, placental abruption, labour induction, C-section	Stillbirth, LBW SGA, RDS Fetal distress Meconium
Vivian-Taylor, 2012 Australia	retrospective cohort *(incidence and comparison)*	604380	2000-2007	Women who gave birth exposed and not exposed to MVC	Linked databases (hospital discharge data & birth/death certificates)	2^{nd}	no	yes	Study-specific definition[3]	Admission, placental abruption, APH,PPH, preterm birth, C-section	Perinatal death (>20^{th} GW), neonatal transfer

Vladutiu, 2013 USA	retrospective cohort *(incidence and comparison)*	878546	2001-2008	Pregnant women 16-46 years, > 20GW, delivering a live/ stillbirth singleton infant	Linked databases (police registry & birth/death certificates)	2nd	yes (seatbelt) yes (airbag)	no	N/A	Placental abruption, PROM, preterm birth	Stillbirth
Weiss, 2002 USA	crash database pregnant vs. non-pregnant (NASS/CDS) *(incidence only)*	32810	1995-1999	Pregnant and non-pregnant women 15–39 years	Sample from population-level database of traffic accidents	any	yes	no	N/A	Maternal death	------------
Weiss, 2008 USA	retrospective cohort *(incidence only)*	1816	1999-2002	Injury-related emergency department visits by pregnant women (only MVC used)	Linked databases (hospital discharge data & birth/death certificates)	any	no	no	N/A	Hospital admission	------------
Whitehead, 2013* USA	PRAMS survey database *(incidence only)*	235329	2000-2005	Survey of women who recently delivered a live-born infant	Population-based cohort (PRAMS)	any	no	no	N/A	Preterm birth, UTI, PROM	------------
Wolf, 1993 USA	population-based retrospective cohort *(incidence only)*	2582	1980-1988	Pregnant women drivers involved in MVC >20GW	Linked databases (police registry & birth/death certificates)	2nd & 3rd	yes	no	N/A	Preterm birth, placental abruption, C-section	Stillbirth, LBW, RDS
Single hospital records/trauma registry											
Aboutanos, 2007 USA	retrospective chart/database review *(incidence only)*	148	2001-2005	Pregnant women presenting to ED following MVC	Single hospital records from trauma centre	any	yes (only in miscarriage)	yes	ISS	Maternal death, miscarriage	Fetal death hydrops fetalis
Baerga-Varela, 2000 USA	retrospective chart/database review *(incidence only)*	39	1986-1996	Admitted to hospital after MVC while pregnant	Single hospital records	any	no	yes	ISS	Maternal death, miscarriage	Stillbirth
Brookfield, 2013 USA	retrospective chart/database review *(incidence only)*	256	1990-2007	Pregnant women presenting to ED following MVC	Single hospital records from trauma centre	any	yes	yes	ISS and RTS	Maternal death, admission to hospital	------------

Chibber, 2015 Kuwait	retrospective chart/database review *(incidence only)*	728	2009-2012	MVC, pregnant, treated at major tertiary hospitals	Single hospital records	2nd	no	no	N/A	Maternal death, placental abruption, preterm birth, uterine rupture, C-Section, admission	Fetal death, fetal distress
Luley, 2013 USA	retrospective chart/database review *(incidence only)*	126	1994-2010	Pregnant women after an MVC >14/40 GA	Single hospital trauma database	2nd & 3rd	yes	no	N/A	Maternal death, placental abruption, C-section	Stillbirth
Miller, 2016 Israel	retrospective cohort *(incidence only)*	3794	2006-2013	Women 18-40 years, in MVC and hospitalized (only pregnant cohort used)	National trauma registry	any	no	no	ISS	Maternal death, miscarriage, placental abruption, C-section	Stillbirth
Orji, 2002 Nigeria	retrospective chart/database review *(incidence only)*	84	1980-2000	Pregnant women in MVC managed in tertiary hospitals	Single hospital records**	any	no	no	N/A	Maternal death, placental abruption, uterine rupture, C-section	Perinatal death (fetal death), fetal tachycardia

*ISS: Injury Severity Score; RTS: Revised Trauma Score; ICU: Intensive Care Unit, N/A not applicable; GA: Gestational Age; LBW: Low birth weight; SGA: Small for gestational age; RDS: Respiratory distress syndrome. *National survey; **Two hospitals in same region included; [1]Possible/probable/incapacitated/fatal; [2]Fatal/major/minor/uninjured; [3]'Severe' = admission to ICU and/or blood transfusion and/or injury to abdomen/pelvis/lower back.*

Table 2. Incidence of adverse outcomes per 1,000 women involved in motor vehicle crashes.

Outcome and study	Number of studies	Number of women	Incidence estimate per 1,000 women	95% CI
Maternal				
Maternal death	**3**	**12000**	**3.60**	**(0.25 to 10.42)**
Azar, 2005			6.57	(4.68 to 8.97)
Kvarnstrand, 2008			6.61	(3.70 to 10.88)
Miller, 2016			0.26	(0.01 to 1.47)
Admission to hospital	**2**	**3838**	**17.08**	**(13.20 to 21.46)**
Vivian-Taylor, 2012			8.90	(5.28 to 14.03)
Weiss, 2008			29.19	(21.94 to 38.0)
Placenta abruption	**6**	**36737**	**16.14**	**(7.04 to 28.78)**
Wolf, 1993			8.10	(5.02 to 12.36)
Miller, 2016			1.05	(0.29 to 2.70)
Schiff, 2005			113.40	(88.80 to 142.01)
Schiff, 2010			12.25	(8.80 to 16.58)
Vivian-Taylor, 2012			16.32	(11.26 to 22.84)
Vladutiu, 2013			7.17	(6.15 to 8.31)
Preterm delivery	**5**	**265680**	**191.90**	**(45.98 to 405.74)**
Schiff, 2005			316.15	(278.53 to 355.65)
Schiff, 2010			97.37	(87.53 to 107.92)
Vivian-Taylor, 2012			83.09	(71.42 to 95.98)
Vladutiu, 2013			110.33	(106.43 to 114.33)
Whitehead, 2013			437.00	(435.00 to 439.01)
PROM	**3**	**260310**	**42.33**	**(5.87 to 109.24)**
Schiff, 2005			22.34	(11.95 to 37.89)
Vladutiu, 2013			23.53	(21.66 to 25.51)
Whitehead, 2013			96.00	(94.81 to 97.20)
Labour induction	**2**	**3930**	**276.43**	**(262.54 to 290.54)**

Schiff, 2005			223.37	(190.15 to 259.42)
Schiff, 2010			286.14	(270.87 to 301.78)
Caesarean section	**5**	**12338**	**166.65**	**(47.34 to 339.00)**
Miller, 2016			6.06	(3.85 to 9.08)
Schiff, 2005			254.30	(219.38 to 291.73)
Schiff, 2010			259.26	(244.48 to 274.46)
Vivian-Taylor, 2012			260.14	(241.13 to 279.85)
Wolf, 1993			171.68	(157.35 to 186.76)
Offspring				
Perinatal death	**8**	**47992**	**6.60**	**(3.81 to 10.12)**
Kvarnstrand, 2008	fetal/neonatal		17.62	(12.62 to 23.92)
Hyde, 2003	fetal		5.01	(3.66 to 6.70)
Miller, 2016	stillbirth		0.79	(0.16 to 2.31)
Schiff, 2005	fetal		12.03	(4.85 to 24.62)
Vivian-Taylor, 2012	stillbirth		16.82	(11.67 to 23.42)
Vladutiu, 2013	stillbirth		5.25	(4.38 to 6.23)
Schiff, 2010	fetal		4.18	(2.29 to 7.01)
Wolf, 1993	fetal		3.47	(1.59 to 6.58)
Fetal distress	**2**	**3930**	**60.09**	**(52.85 to 67.77)**
Schiff, 2005			132.30	(105.84 to 162.56)
Schiff, 2010			50.48	(43.31 to 58.44)
Meconium at delivery	**2**	**3930**	**52.61**	**(45.82 to 59.85)**
Schiff, 2005			63.57	(45.15 to 86.57)
Schiff, 2010			51.08	(43.86 to 59.08)
RDS	**3**	**6522**	**15.19**	**(5.83 to 28.68)**
Schiff, 2005			32.65	(19.77 to 50.51)
Schiff, 2010			14.64	(10.85 to 19.30)
Wolf, 1993			6.17	(3.53 to 10.00)

***Data source: population database**; CI, Confidence Interval; PROM: Premature Rupture of Membranes; RDS: Respiratory Distress Syndrome.*

Figures

Figure 1. The study selection process in the systematic review of outcomes on pregnant women involved in motor vehicle crashes

Figure 2. The quality assessment of the included studies

Figure 3. Comparison of outcomes between women involved and not involved in motor vehicle crashes

Figure 1. (Supplementary). Comparison of pregnancy complications between women involved and not involved in motor vehicle crashes stratified by seatbelt use

Figure 2. (Supplementary). Comparison of fetal death between women involved and not involved in motor vehicle crashes stratified by seatbelt use

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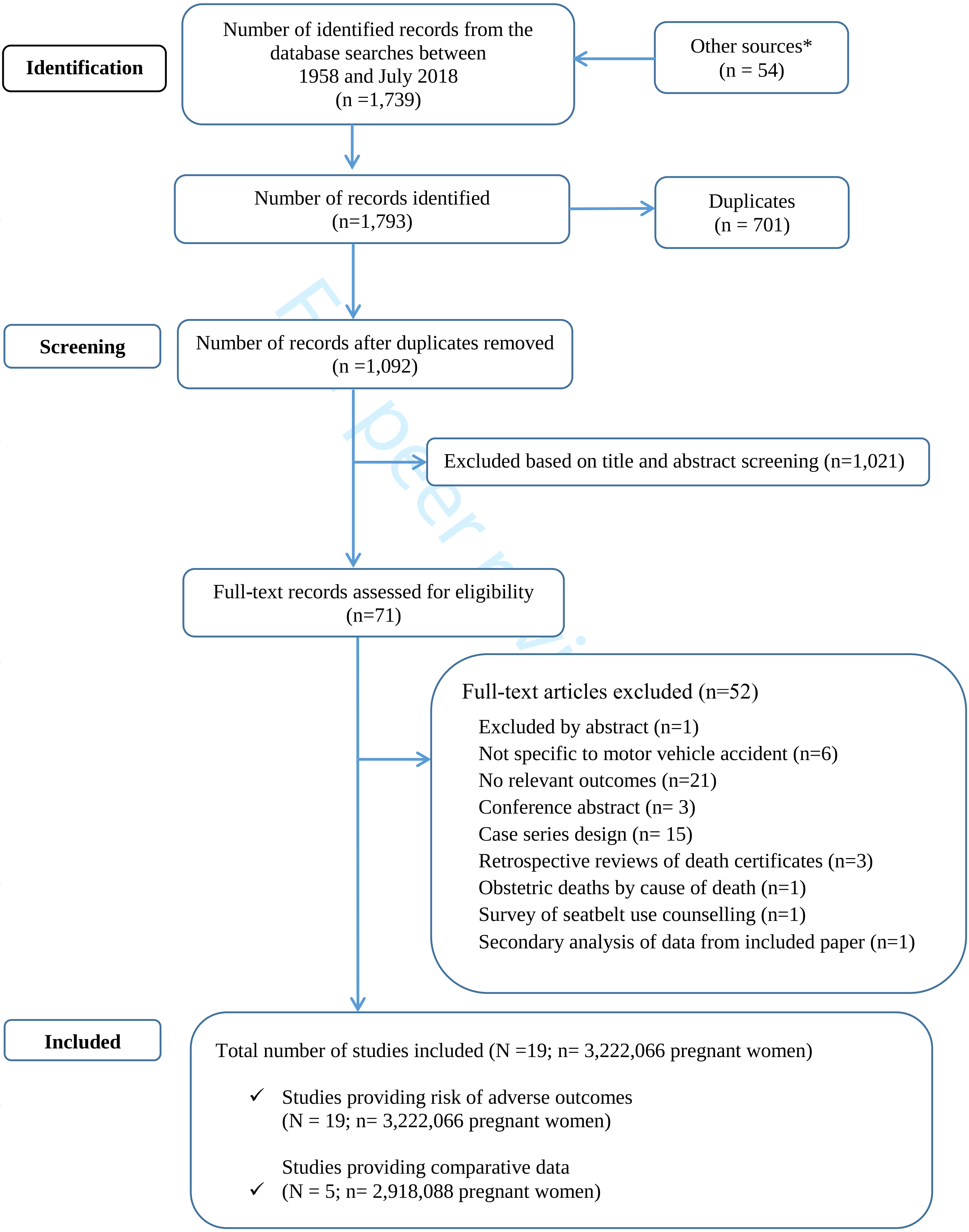
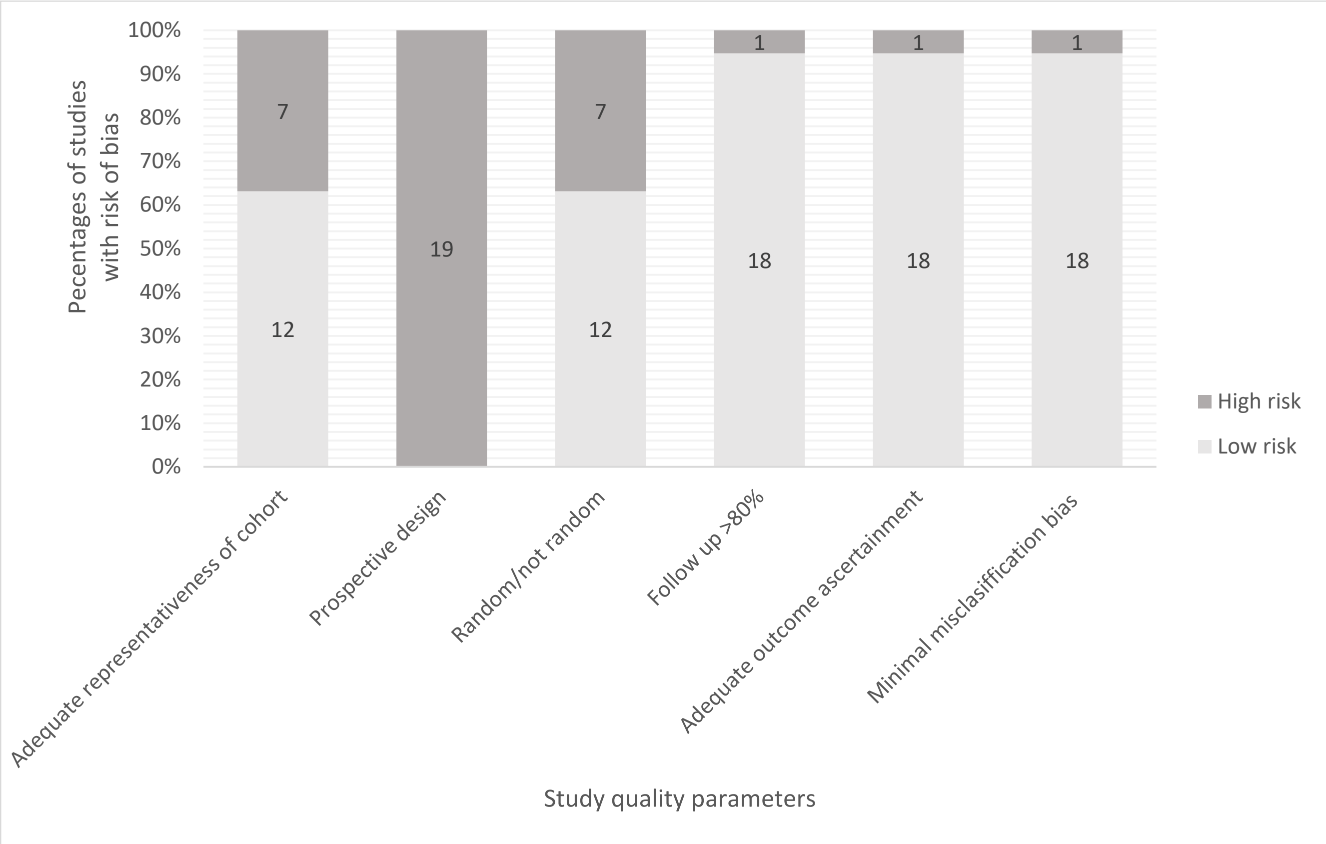


**references of relevant non-systematic reviews and Google scholar*



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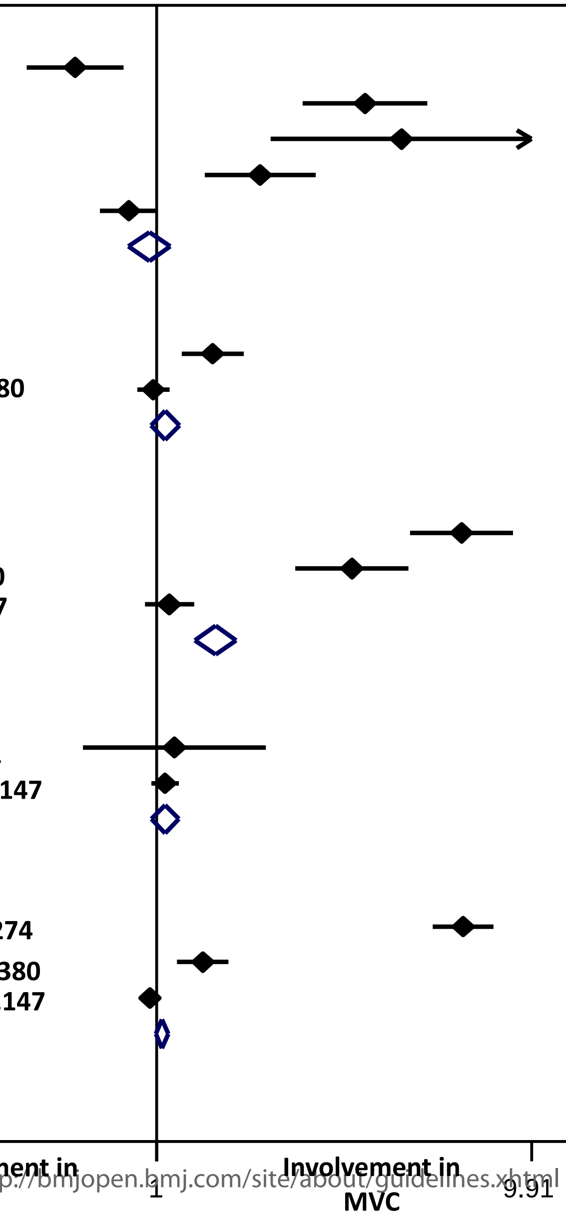
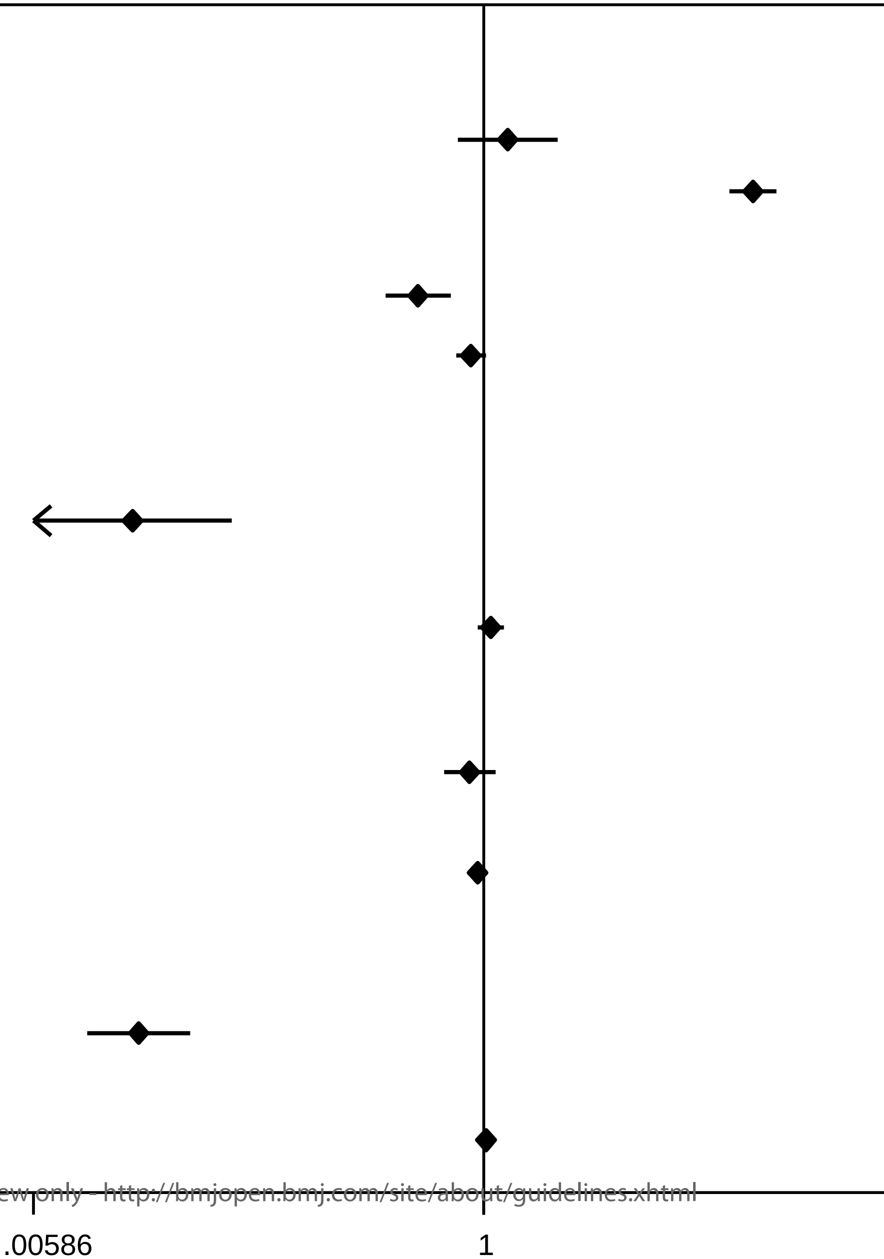
1
18
High risk
Low risk
Adequate representativeness of cohort
Prospective design
Random/not random
Follow up >80%
Adequate outcome ascertainment
Minimal misclasiffication bias
Study quality parameters

Outcome / Study ID	Events/exposed	Events/non-exposed	OR (95% CI) Random-effects	Weight %
Perinatal death				
Hyde, 2003	45/8,985	2,600/316,274	0.61 (0.45 to 0.82)	29.18
Kvarnstrand, 2008	27/2,270	3,668/1,092,262	3.57 (2.44 to 5.23)	3.07
Schiff, 2005	7/582	47/17,274	4.46 (2.01 to 9.91)	0.62
Vivian-Taylor, 2012	34/2,022	5,439/604,380	1.88 (1.34 to 2.65)	7.28
Vladutiu, 2013a	128/24,399	5,305/854,147	0.84 (0.71 to 1.01)	59.85
Subtotal (I^2 = 95.4%, p = 0.000)			**0.96 (0.84 to 1.09)**	100.00
Cesarean delivery				
Schiff, 2005	148/582	3,367/17,274	1.41 (1.16 to 1.70)	17.21
Vivian-Taylor, 2012	526/2,022	159,556/604,380	0.98 (0.89 to 1.08)	82.79
Subtotal (I^2 = 90.9%, p = 0.001)			**1.05 (0.97 to 1.15)**	100.00
Placental abruption				
Schiff, 2005	50/582	248/17,274	6.45 (4.70 to 8.85)	4.25
Vivian-Taylor, 2012	33/2,022	3,022/604,380	3.30 (2.34 to 4.67)	5.70
Vladutiu, 2013a	175/24,399	5,680/854,147	1.08 (0.93 to 1.25)	90.05
Subtotal (I^2 = 98.4%, p = 0.000)			**1.43 (1.27 to 1.63)**	100.00
Premature Rupture of Membranes				
Schiff, 2005	13/582	347/17,274	1.11 (0.64 to 1.95)	2.09
Vladutiu, 2013a	574/24,399	19,126/854,147	1.05 (0.97 to 1.14)	97.91
Subtotal (I^2 = 0.0%, p = 0.841)			**1.05 (0.97 to 1.14)**	100.00
Preterm delivery				
Schiff, 2005	184/582	1,143/316,274	6.52 (5.42 to 7.85)	1.00
Vivian-Taylor, 2012	168/2,022	38,681/604,380	1.33 (1.13 to 1.55)	4.62
Vladutiu, 2013a	2,692/24,399	97,737/854,147	0.96 (0.92 to 1.00)	94.38
Subtotal (I^2 = 99.5%, p = 0.000)			**1.03 (0.99 to 1.07)**	100.00



Outcome / *Study ID*	Overall incidence	Study size	OR (95% CI)
Fetal death			
Seatbelts not used			
Hyde, 2003	*1.176*	*2222*	1.32 (0.74 to 2.33)
Vladutiu, 2013a	*5.333*	*1006*	21.65 (16.51 to 28.39)
Seatbelts used			
Hyde, 2003	*.1832*	*14346*	0.47 (0.33 to 0.69)
Vladutiu, 2013a	*.1102*	*49328*	0.87 (0.73 to 1.03)
Placental abruption			
Seatbelts not used			
Vladutiu, 2013a	*.1152*	*49328*	0.02 (0.01 to 0.06)
Seatbelts used			
Vladutiu, 2013a	*.1188*	*49328*	1.09 (0.93 to 1.26)
Preterm delivery			
Seatbelts not used			
Vladutiu, 2013a	*97.2*	*1006*	0.85 (0.64 to 1.14)
Seatbelts used			
Vladutiu, 2013a	*2.035*	*49328*	0.94 (0.90 to 0.97)
Premature Rupture Of Membranes			
Seatbelts not used			
Vladutiu, 2013a	*.388*	*49328*	0.02 (0.01 to 0.04)
Seatbelts used			
Vladutiu, 2013a	*.3993*	*49328*	1.03 (0.95 to 1.12)



Study ID (Subgroup)	MVC Events	MVC Total	Non MVC Events	Non MVC Total	Weight	Odds Ratio M-H, Random, 95% CI
Fetal deaths (seatbelts used)						
Hyde 2003	28	7145	2600	313674	46.2%	0.47 (0.32 to 0.68)
Vladutiu 2013	133	24531	5305	848073	53.8%	0.87 (0.73 to 1.03)
Subtotal (95% CI)		**31676**		**1161747**	**100.0%**	**0.65 (0.36 to 1.19)**
Total events	**161**		**7905**			
Fetal death (seatbelts not used)						
Hyde 2003	12	1099	2600	313674	49.8%	1.32 (0.75 to 2.34)
Vladutiu 2013	60	443	5305	848073	50.2%	24.89 (18.93 to 32.71)
Subtotal (95% CI)		**1542**		**1161747**	**100.0%**	**5.78 (0.17 to 201.12)**
Total events	**72**		**7905**			

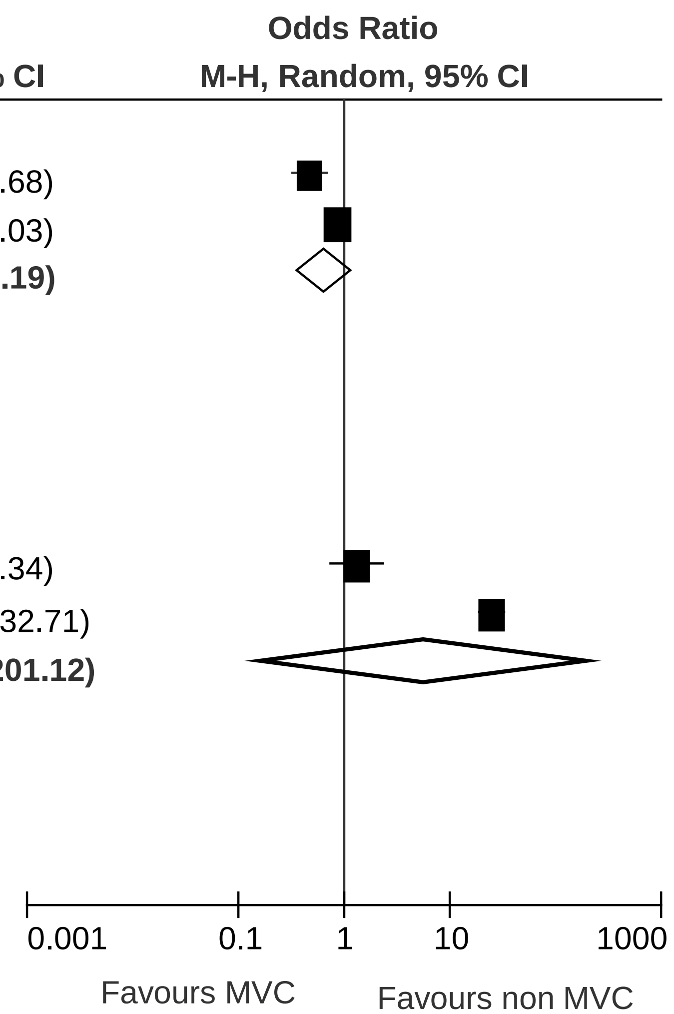
Fetal deaths (seatbelts used): Heterogeneity: $Tau^2 = 0.17$; $Chi^2 = 8.58$, df = 1 (P = 0.003); $I^2 = 88\%$

Test for overall effect: Z = 1.39 (P = 0.16)

Fetal death (seatbelts not used): Heterogeneity: $Tau^2 = 6.51$; $Chi^2 = 126.07$, df = 1 (P < 0.00001); $I^2 = 99\%$

Test for overall effect: Z = 0.97 (P = 0.33)

Test for subgroup differences: $Chi^2 = 1.41$, df = 1 (P = 0.24), $I^2 = 28.9\%$



*MVC, motor vehicle crash

Appendix 1. Search strategy for MEDLINE (via Ovid) executed from database inception up to July 2018

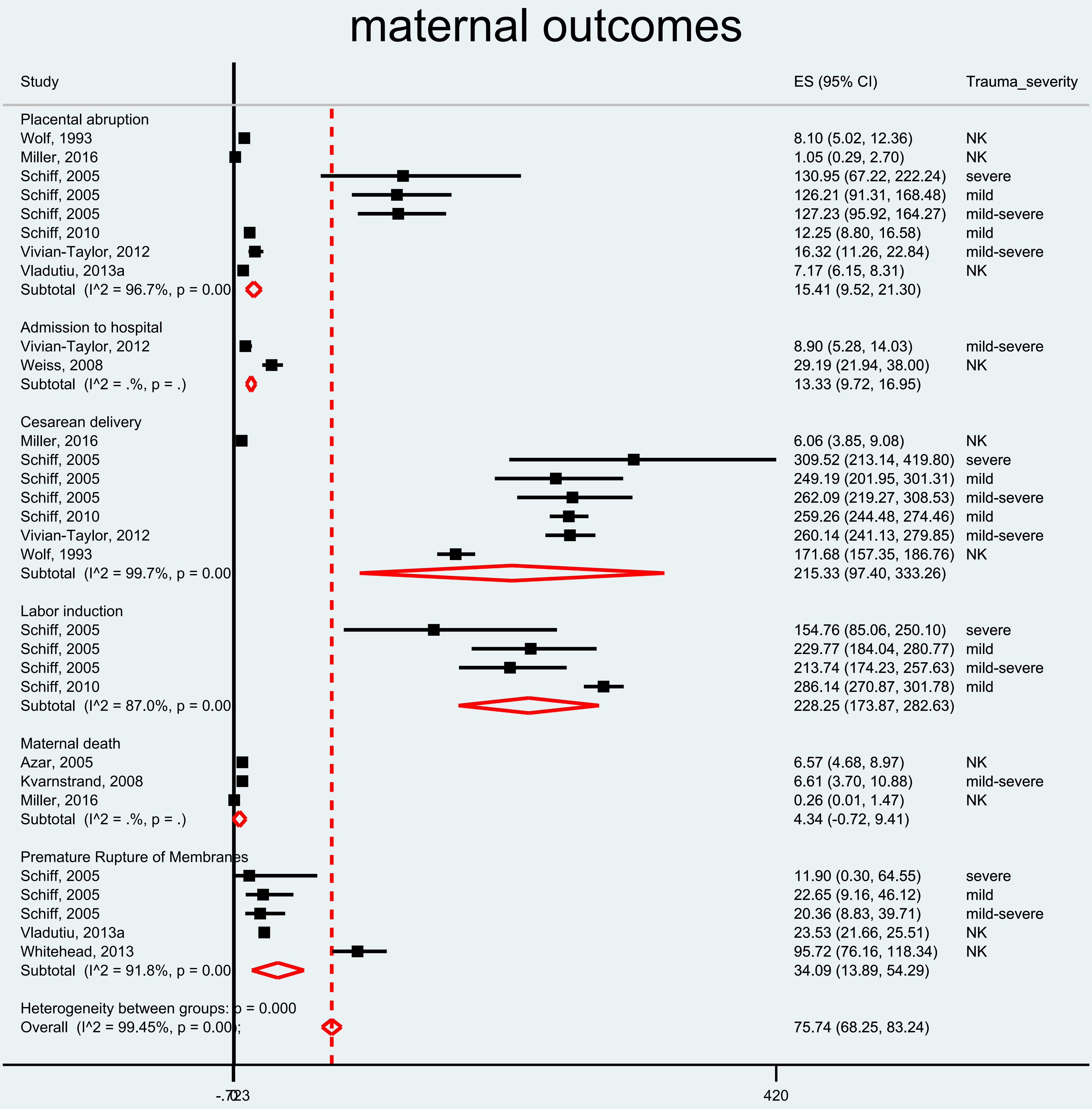
Item	Search term
1	pregnancy.af.
2	pregnan*.sh.
3	gravidity.sh.
4	gravid*.sh.
5	gestation*.sh.
6	pregnant women.sh.
7	pregnant wom#n.sh.
8	(child adj3 bearing).tw.
9	childbearing.af.
10	matern*.sh.
11	vehicle* crash*.af.
12	vehicle* accident*.af.
13	vehicle* collision*.af.
14	motor vehicle crash*.af.
15	motor vehicle accident*.af.
16	motor vehicle collision*.af.
17	motor vehicle injur*.af.
18	vehicle* injur*.af.
19	road traffic crash*.af.
20	road traffic accident*.af.
21	road traffic collision*.af.
22	road traffic injur*.af.
23	auto* crash*.af.
24	auto* accident*.af.
25	auto* collision*.af.
26	auto* injur*.af.
27	car crash*.af.
28	car accident*.af.
29	car collision*.af.
30	car injur*.af.
31	(car adj3 trauma).af.
32	(automobile adj3 trauma).af.
33	(automotive adj3 trauma).af.
34	(road traffic adj3 trauma).af.
35	(motor vehicle adj3 trauma).af.
36	1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10
37	11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34 or 35
38	36 and 37

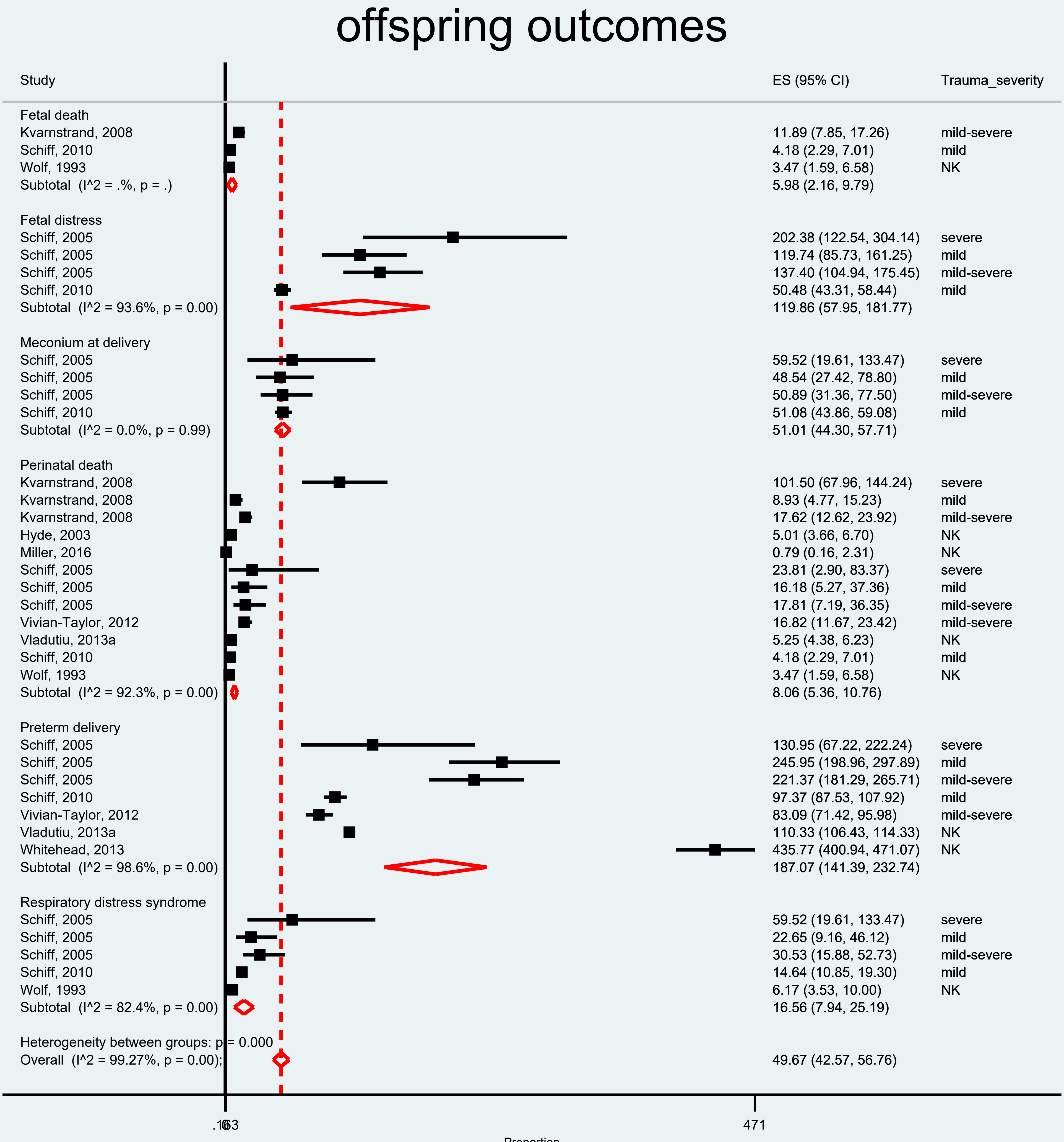
Appendix 2 List of excluded studies with reasons

Study ID	Reason	Reference
Al Mulhim, 2012	Pregnancy loss or not after trauma in Arabic pregnant women	*EMHJ. Vol. 18 No. 5 2012*
Battaloglu 2016	From a cohort of 15,140 female patients, 173 were pregnant women in the trauma registry. 55.5% of them from vehicle collision	**SR Petrone, 2017** *Injury, Int. J. Care Injured 47 (2016) 184-187*
Barre 2006	Pregnant women with abdominal trauma during pregnancy (n=65). Half of them from a traffic accident.	**SR Petrone, 2017** *La Revue Sage-Femme. Vol 5, Issue 6, 2006, 312-316*
Cannada 2010	Pregnant women with orthopaedic injuries (n=65)	**SR Petrone, 2017** *Injury, Infection, and Critical Care.2010. Vol. 69 (3)*
Chamberlain, 2011	Communication abstract. Retrospective cohort study. Identification of 272 pregnant trauma victims. 78.6% of them incurred in a MVC. No data to extract	*American Journal of Obstetrics & Gynecology Supplement to January 2011*
Cheng, 2012	Maternal complications during delivery according to uninjured, minor and severe injuries. 2,881 pregnant women (47,4%) involved in MVC	*World J Surg (2012) 36:2767–2775*
Connolly, 1997	476 maternal records of trauma cases. 54.6% were MVC. No more data available	*American Journal of Perinatology.1997.Vol. 14 (6)*
Corsi 1999	Twenty-seven traumatised pregnant women were analysed retrospectively over a period of 9 years in Sao Paulo, Brazil	**SR Petrone, 2017** *Injury, Int. J. Care Injured 30 (1999) 239-243*
Dannenberg, 1995	Homicide and other injuries as causes of maternal death between 1987 and 1991 in New York	*Am J Obstet Gynecol Vol.172 (5)*
Deshpande, 2017	Trauma impact on maternal mortality. Comparability between pregnant vs. non pregnant women	*American Journal of Obstetrics & Gynecology 2017. 590.e2*
El Kady 2004	Retrospective cohort study of women hospitalized for Trauma in California	**SR Petrone, 2017** *American Journal of Obstetrics and Gynecology (2004) 190, 1661-8*
El Kady D, 2006	Fractures injuries on maternal/neonatal outcomes in United States	**SR Méndez -Figueroa 2013** *American Journal of Obstetrics and Gynecology (2006) 195, 711–6*
Fischer 2011	Minor trauma and poor fetal outcomes in Tennessee, Memphis	**SR Petrone, 2017** *Injury, Infection, and Critical Care. 2011. Vol. 71 (1)*
Gibbins, 2017	Communication. MVC and Stillbirth. Secondary analysis of 439 stillbirth	American Journal of Obstetrics & Gynecology Supplement to January 2017
Goodwin, 1990	Case-series of trauma pregnant women between 1987 and 1988 in Los Angeles	**SR Méndez -Figueroa 2013** *Am J Obstet Gynecol. 1990 Vol. 162 (3).*
Hardt, 2013	Prenatal risk screening to identify women at increased risk for traumatic pregnancy-	*Women's Health Issues 23-3 (2013) e187–e193*

	associated death	
Hardy, 1974	Maternal mortality ratios at large urban charity hospitals from 1941 to 1971	*Obstetric and Gynecology. 1974. Vol.43 (1)*
Harland 2014	Risks factors of maternal injuries in a population-based sample of pregnant women from Iowa	**SR Petrone, 2017** *Journal of Women's Health. 2014. Vol. 23 (12)*
Hitosugi 2006	135 traffic accidents involving Japanese pregnant women from insurance companies. The outcomes of neonates determined by their condition 1 month after birth (death/abortion/healthy)	**SR Petrone, 2017** *Forensic Science International 159 (2006) 51-54*
Ikossi, 2005	Risks factors of trauma in pregnant women from San Francisco, California	*J Am Coll Surg. Vol. 2005. 200 (1)*
Lynch, 2011	Pregnancy associated- death in Ohio: 2003-2007	American Journal of Obstetrics & Gynecology Supplement to January 2011
Manoogian, 2015	Injuries characteristics between pregnant vs non pregnant women occupants (not outcome)	*Accident Analysis and Prevention 74 (2015). 69–76*
Melamed 2012	Outcomes following blunt trauma in Pregnant women from Israel	**SR Petrone, 2017** *The Journal of Maternal-Fetal and Neonatal Medicine. 2012; 25(9): 1612–1617*
Mesdaghinia, 2012	Causes of trauma in 32 pregnant women with trauma in a Hospital in Iran	*Arch Trauma Res. 2012;1(1):23-26*
Nannini, 2008	Risks of injury in pregnant women in Massachusets	*Journal of Midwifery & Women's Health.2008. Vol.53 (1)*
Omoke, 2013	Trauma during pregnancy in a Nigerian setting	*Int J Crit Illn Inj Sci. 2013; 3(4): 269–273.*
Osei-Ampofo, 2016	A cross-sectional study with 134 pregnant women from Ghana visiting the emergency care. Leading injury MVC (23%). Not outcomes	*African Journal of Emergency Medicine (2016) 6, 87 –93*
Pak, 1998	Delivery outcomes after a blunt abdominal trauma in 85 pregnant women	*Am J Obstet Gynecol. 1998. Vol. 179 (5)*
Patteson, 2007	High risk factors involved in trauma during pregnancy. Not outcomes	*The Journal of TRAUMA Injury, Infection, and Critical Care. 2007. Vol 62 (4)*
Pearlman, 1990	Not possible to assess full text	SR Méndez -Figueroa 2013
Schiff, 1997	Seat Bealt use. Protective factor of maternal mortality after a MVC in Mexico	*WJM, 1997. Vol. 167 (1)*
Schuster, 2016	Communication abstract. Impact of blunt trauma on maternal and pregnancy outcome. MVC the most common injury mechanism (70%). Pennsylvania Trauma Systems Foundation Database (1996-2013).	*American Journal of Obstetrics & Gynecology. Supplement to January 2016*
Schuster, 2018	Pennsylvania Trauma Systems Foundation Database. ISS>9 and SBP<90mmHg are predictors for poor outcomes after trauma during pregnancy	*Trauma, 2018. Vol. 20(1) 30–37*
Sela, 2011	Treatment provided to pregnant motor vehicle accident (MVA) casualties in a mature trauma system in Israel	*Annals of Surgery, 2011.Vol.254 (2)*

Shah, 1998	Trauma in general in pregnant women	*J Trauma. 1998 Jul;45(1):83-6*
Shakerian 2015	Determining adherence to recommended imaging guidelines in pregnant women from Victoria, Australia	**SR Petrone, 2017** *J Trauma Acute Care Surg. 2015.Vol. 78 (1)*
Shiff 2002	Retrospective cohort study to assess outcomes of pregnant women hospitalized for injury in Washington State from 1989 to 1997	**SR Petrone, 2017** *J Trauma. 2002; 53: 939–945.*
Sirin, 2007	Report the prevalence of seatbelt counselling by prenatal care providers during pregnancy in USA	*Matern Child Health J (2007) 11:505–510*
Tinker 2010	Risks factors involved in injuries in pregnant women from the National Birth Defects Prevention Study, USA	**SR Petrone, 2017** *Journal of Women's Health. 2010. Vol. 19 (2)*
Van der Knoop, 2015	Effect of maternal trauma in fetal motility at term and at one year of age	*Early Human Development 91 (2015) 511–517*
Van der Knoop, 2018	Matched case-control study. Neurobehavioral outcome in 6-18 year old children after trauma in pregnancy	*European Journal of Paediatric Neurology (2018), 22(5):845-853*
Vladutiu, 2013b	Same sample Vladutiu 2013a; excluded as a secondary analysis from already included study	*Accid Anal Prev. 2013; 55: 165–171*
Wahabi, 2007	45 MVC case series pregnant women collected over a 10- year period	*Saudi Med J. 2007. Vol. 28 (9)*
Wall 2014	Pregnant trauma patiens from South Africa (mainly assaults)	**SR Petrone, 2017** *Injury, Int. J. Care Injured 45 (2014) 1220–1223*
Weiner 2016	Minor trauma during pregnancy, not associated with adverse pregnancy outcomes, Israel	**SR Petrone, 2017** *European Journal Of Obstetrics & Gynecology and Reproductive Biology 203 (2016): 78–81*
Weiss, 1999	Retrospect review of death certificates	*43rd Annual Proceedings Association for the Advancement of Automotive Medicine September 20-21, 1999. Barcelona (Sitges), Spain*
Weiss, 2001	Retrospect review of death certificates	*JAMA, 2001. Vol. 286 (15)*
Weiss, 2002a	N/A	
Zangene, 2015	102 cases of trauma in pregnancy registered in Iran from 2007 to 2010. MVC the most frequent (45%)	*Global Journal of Health Science. 2015. Vol 7 (2)*


maternal outcomes
Study
ES (95% CI)
Trauma_severity
Placental abruption
Wolf, 1993 | 8.10 (5.02, 12.36) | NK
Miller, 2016 | 1.05 (0.29, 2.70) | NK
Schiff, 2005 | 130.95 (67.22, 222.24) | severe
Schiff, 2005 | 126.21 (91.31, 168.48) | mild
Schiff, 2005 | 127.23 (95.92, 164.27) | mild-severe
Schiff, 2010 | 12.25 (8.80, 16.58) | mild
Vivian-Taylor, 2012 | 16.32 (11.26, 22.84) | mild-severe
Vladutiu, 2013a | 7.17 (6.15, 8.31) | NK
Subtotal (I^2 = 96.7%, p = 0.00 | 15.41 (9.52, 21.30)
Admission to hospital
Vivian-Taylor, 2012 | 8.90 (5.28, 14.03) | mild-severe
Weiss, 2008 | 29.19 (21.94, 38.00) | NK
Subtotal (I^2 = .%, p = .) | 13.33 (9.72, 16.95)
Cesarean delivery
Miller, 2016 | 6.06 (3.85, 9.08) | NK
Schiff, 2005 | 309.52 (213.14, 419.80) | severe
Schiff, 2005 | 249.19 (201.95, 301.31) | mild
Schiff, 2005 | 262.09 (219.27, 308.53) | mild-severe
Schiff, 2010 | 259.26 (244.48, 274.46) | mild
Vivian-Taylor, 2012 | 260.14 (241.13, 279.85) | mild-severe
Wolf, 1993 | 171.68 (157.35, 186.76) | NK
Subtotal (I^2 = 99.7%, p = 0.00 | 215.33 (97.40, 333.26)
Labor induction
Schiff, 2005 | 154.76 (85.06, 250.10) | severe
Schiff, 2005 | 229.77 (184.04, 280.77) | mild
Schiff, 2005 | 213.74 (174.23, 257.63) | mild-severe
Schiff, 2010 | 286.14 (270.87, 301.78) | mild
Subtotal (I^2 = 87.0%, p = 0.00 | 228.25 (173.87, 282.63)
Maternal death
Azar, 2005 | 6.57 (4.68, 8.97) | NK
Kvarnstrand, 2008 | 6.61 (3.70, 10.88) | mild-severe
Miller, 2016 | 0.26 (0.01, 1.47) | NK
Subtotal (I^2 = .%, p = .) | 4.34 (-0.72, 9.41)
Premature Rupture of Membranes
Schiff, 2005 | 11.90 (0.30, 64.55) | severe
Schiff, 2005 | 22.65 (9.16, 46.12) | mild
Schiff, 2005 | 20.36 (8.83, 39.71) | mild-severe
Vladutiu, 2013a | 23.53 (21.66, 25.51) | NK
Whitehead, 2013 | 95.72 (76.16, 118.34) | NK
Subtotal (I^2 = 91.8%, p = 0.00 | 34.09 (13.89, 54.29)
Heterogeneity between groups: p = 0.000
Overall (I^2 = 99.45%, p = 0.00); | 75.74 (68.25, 83.24)
-.723
0
420
Proportion


offspring outcomes
Study
ES (95% CI)
Trauma_severity
Fetal death
Kvarnstrand, 2008 | 11.89 (7.85, 17.26) | mild-severe
Schiff, 2010 | 4.18 (2.29, 7.01) | mild
Wolf, 1993 | 3.47 (1.59, 6.58) | NK
Subtotal (I^2 = .%, p = .) | 5.98 (2.16, 9.79)
Fetal distress
Schiff, 2005 | 202.38 (122.54, 304.14) | severe
Schiff, 2005 | 119.74 (85.73, 161.25) | mild
Schiff, 2005 | 137.40 (104.94, 175.45) | mild-severe
Schiff, 2010 | 50.48 (43.31, 58.44) | mild
Subtotal (I^2 = 93.6%, p = 0.00) | 119.86 (57.95, 181.77)
Meconium at delivery
Schiff, 2005 | 59.52 (19.61, 133.47) | severe
Schiff, 2005 | 48.54 (27.42, 78.80) | mild
Schiff, 2005 | 50.89 (31.36, 77.50) | mild-severe
Schiff, 2010 | 51.08 (43.86, 59.08) | mild
Subtotal (I^2 = 0.0%, p = 0.99) | 51.01 (44.30, 57.71)
Perinatal death
Kvarnstrand, 2008 | 101.50 (67.96, 144.24) | severe
Kvarnstrand, 2008 | 8.93 (4.77, 15.23) | mild
Kvarnstrand, 2008 | 17.62 (12.62, 23.92) | mild-severe
Hyde, 2003 | 5.01 (3.66, 6.70) | NK
Miller, 2016 | 0.79 (0.16, 2.31) | NK
Schiff, 2005 | 23.81 (2.90, 83.37) | severe
Schiff, 2005 | 16.18 (5.27, 37.36) | mild
Schiff, 2005 | 17.81 (7.19, 36.35) | mild-severe
Vivian-Taylor, 2012 | 16.82 (11.67, 23.42) | mild-severe
Vladutiu, 2013a | 5.25 (4.38, 6.23) | NK
Schiff, 2010 | 4.18 (2.29, 7.01) | mild
Wolf, 1993 | 3.47 (1.59, 6.58) | NK
Subtotal (I^2 = 92.3%, p = 0.00) | 8.06 (5.36, 10.76)
Preterm delivery
Schiff, 2005 | 130.95 (67.22, 222.24) | severe
Schiff, 2005 | 245.95 (198.96, 297.89) | mild
Schiff, 2005 | 221.37 (181.29, 265.71) | mild-severe
Schiff, 2010 | 97.37 (87.53, 107.92) | mild
Vivian-Taylor, 2012 | 83.09 (71.42, 95.98) | mild-severe
Vladutiu, 2013a | 110.33 (106.43, 114.33) | NK
Whitehead, 2013 | 435.77 (400.94, 471.07) | NK
Subtotal (I^2 = 98.6%, p = 0.00) | 187.07 (141.39, 232.74)
Respiratory distress syndrome
Schiff, 2005 | 59.52 (19.61, 133.47) | severe
Schiff, 2005 | 22.65 (9.16, 46.12) | mild
Schiff, 2005 | 30.53 (15.88, 52.73) | mild-severe
Schiff, 2010 | 14.64 (10.85, 19.30) | mild
Wolf, 1993 | 6.17 (3.53, 10.00) | NK
Subtotal (I^2 = 82.4%, p = 0.00) | 16.56 (7.94, 25.19)
Heterogeneity between groups: p = 0.000
Overall (I^2 = 99.27%, p = 0.00); | 49.67 (42.57, 56.76)
.163
471
Proportion

Appendix 5. Incidence of maternal, fetal & neonatal complications from single studies

Outcome	Total sample size	Incidence estimate per 1,000 women (95%CI)
Maternal outcomes		
Placental problems	235329	100.00 (98.79, 101.22)
Miscarriage	3794	1.85 (0.74, 3.80)
Antepartum haemorrhage	2022	47.48 (38.62, 57.67)
Postpartum haemorrhage	2022	77.65 (66.35, 90.18)
Vaginal bleeding	235329	247.00 (245.26, 248.75)
Hospital stay >=6 days	5936	117.92 (109.82, 126.40)
Maternal death or hospitalisation	32810	135.05 (131.37, 138.80)
Fetal and neonatal		
Hypoxia	582	22.34 (11.95, 37.89)
Neonatal death	2270	5.73 (3.05, 9.77)
Neonatal transfer	2022	42.53 (34.16, 52.26

Appendix 6. Incidence in non-population level data

Outcome	Study ID	Number of events	Group size	Trauma severity level
Admission to hospital	Brookfield, 2013	182	256	Not given
	Chibber, 2015	648	728	Not given
Caesarean delivery	Chibber, 2015	529	728	Not given
	Luley 2013	32	126	Not given
	Orji, 2002	2	84	Not given
Fetal death	Aboutanos, 2007	1	148	Not given
	Chibber, 2015	78	728	Not given
Fetal distress	Chibber, 2015	412	728	Not given
Fetal tachycardia	Orji, 2002	10	84	Not given
Hydrops fetalis	Aboutanos, 2007	1	148	Not given
Maternal death	Aboutanos, 2007	0	148	Not given
	Baerga-Varela, 2000	1	39	Severe
	Brookfield, 2013	7	256	Not given
	Chibber, 2015	100	728	Not given
Maternal death	Orji, 2002	2	84	Not given
Miscarriage	Aboutanos, 2007	5	148	Not given
	Baerga-Varela, 2000	7	39	Mild to severe
Perinatal death	Baerga-Varela, 2000	23	39	Mild to severe
	Luley 2013	6	126	Not given
	Orji, 2002	3	84	Not given
Placental abruption	Chibber, 2015	428	728	Not given
	Luley 2013	7	126	Not given
	Orji, 2002	1	84	Not given
Preterm delivery	Chibber, 2015	97	728	Not given
Uterine rupture	Chibber, 2015	12	728	Not given
	Orji, 2002	1	84	Not given

PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	2-3
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	4
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	5
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	5
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	5-7
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	5
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	**Appendix 1**
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	5-6, **Appendix 2**
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	6-7
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	5-7
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	7
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	7-8
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	8

PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	7-8
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	7-8
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	8, **Figure 1**
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	8, **Table 1**
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	8, 9, **Figure 2**
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	9,10 **Table 2, Figure 3** **Figure S1,S2** **Appendix 5, 6**
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	10, **Appendix 3, 4**
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	8,9 **Figure 2**
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	9,10 **Figure S1, S2**
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	10
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	11

PRISMA 2009 Checklist

Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	12
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	3

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed1000097

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Maternal trauma due to motor vehicle crashes and pregnancy outcomes: A systematic review and meta-analysis

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Maternal trauma due to motor vehicle crashes and pregnancy outcomes: A systematic review and meta-analysis

Amezcua-Prieto C [1,2,3], Ross J[4], Rogozińska E,[5,6] Mighiu P[5], Martínez-Ruiz V[1,2,3], Brohi K[4], Bueno-Cavanillas A[1,2,3], Khan KS[1,5], Thangaratinam S[5]*

[1]*Department of Preventive Medicine and Public Health. Faculty of Medicine. University of Granada. Avenida de la Investigación, 11; 18071 Granada, Spain*
[2]*CIBER de Epidemiología y Salud Pública. (CIBERESP), Granada, Spain*
[3]*Instituto de Investigación Biosanitaria ibs.GRANADA, Granada, Spain*
[4]*Centre for Trauma Sciences, Queen Mary University of London, London, United Kingdom*
[5]*Women's Health Research Unit, Barts and the London School of Medicine and Dentistry, London, United Kingdom*
[6]*Meta-analysis Group, MRC Clinical Trials Unit, University College London, London, United Kingdom*

Correspondence to:
Aurora Bueno-Cavanillas, PhD, Professor
Professor of Preventive Medicine and Public Health
Department of Preventive Medicine and Public Health, Faculty of Medicine, The University of Granada, Avenida de la Investigación, 11; 18016 Granada, Spain
CIBER de Epidemiología y Salud Pública. (CIBERESP), Granada, Spain,
Instituto de Investigación Biosanitaria ibs.GRANADA, Granada, Spain
Email: abueno@ugr.es

Abstract

Objectives

To systematically review and quantify the effect of motor vehicle crashes (MVC) in pregnancy on maternal and offspring outcomes.

Design

Systematic review and meta-analysis of observational data searched from inception until July 1, 2018. Searching was from June to August 2018 in Medline, Embase, Web of Science, Scopus, LILACS SciELO, TRANSPORT, IRRD, TRANSDOC, CDSR, and Cochrane Central Register CENTRAL.

Participants

Studies were selected if they focused on the effects of exposure MVC during pregnancy vs. non-exposure, with follow up to verify outcomes in various settings, including secondary care, collision and emergency, and inpatient care.

Data synthesis

For incidence data, we calculated a pooled estimate per 1,000 women. For comparison of outcomes between women involved and those not involved in MVC, we calculated odds ratios with 95% confidence intervals. Where possible, we statistically pooled the data using the random-effects model. The quality of studies used in the comparative analysis was assessed with Newcastle-Ottawa Scale.

Results

We included 19 studies (3,222,066 women) of which the majority was carried out in high-income countries (18/19). In population-level studies of women involved in MVC, maternal death occurred in 3.6 per 1,000 (95% CI 0.25 to 10.42; 3 studies, 12,000 women; Tau= 1.77), and fetal death or stillbirth in 6.6 per 1,000 (95% CI 3.81 to 10.12; 8 studies, 47,992 women; I^2=92.6%). Pooled incidence of complications per 1,000 women involved in MVC was labour induction (276.43), preterm delivery (191.90) and caesarean section (166.65). Compared to women not involved in MVC, those involved had increased odds of placental abruption (OR 1.43, 95% CI 1.27 to 1.63; 3 studies, 1,500,825 women) and maternal death (OR 202.27; 95% CI 110.60 to 369.95; 1 study, 1,094,559 women).

Conclusion: Pregnant women involved in MVC were at higher risk of maternal death and complications than those not involved.

PROSPERO registration: CRD42018100788

Key terms: Pregnancy; motor vehicle crashes; pregnancy complications

Word count: 300

Strengths and limitations of this study

- This is the first systematic review examining the link between involvement in MVC, mortality and adverse outcomes that includes evaluation of study quality assessment.
- This is the second systematic review looking at outcomes following MVC in pregnancy.
- We conducted our review using a prospectively registered protocol and reported it in accordance with the international standards.
- Outcomes variables correspond to any trimester, not to specific trimesters.
- Outcomes according to seatbelt use are scarce, since only two studies use population-level data.

Funding statement

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Competing interest's statement

There are non-financial associations that may be relevant to the submitted manuscript.

Introduction

Up to half of all women in developed countries drive motor vehicles (1) and the consequences of road traffic-related injuries involving pregnant women can be severe (2). Indeed, motor vehicle crashes (MVC) are the most common cause of non-obstetric trauma associated with fetal deaths (2.3 per 100,000 live births) (3) . The risk of adverse outcomes resulting from an MVC increases in the second trimester of pregnancy if the pregnant women were the driver (4); however, this does not appear to be the case for pregnant passengers or pedestrians (5). A maternal mortality rate of 3.5 women per 100,000 is reported following MVCs in pregnant women (6). Mechanisms of injury recorded within the pregnant population of the UK national trauma registry, the Trauma Audit and Research Network (TARN), saw an increased rate of vehicular collision in pregnant women when compared to the non-pregnant cohort (7). In 2001-2008, 2.9% of pregnant women in North Carolina were drivers in one or more crashes (8). In the USA, data from the National Automotive Sampling System (NASS/CDS) reflects that when vehicles with pregnant women are involved in collision, 50% of those women will sustain an injury(9). There are few safety guidelines on travelling by car during pregnancy (10-12). The focus of these tends to be on questions around the use of seatbelts and the activation of airbags in the car (12).

There is a reported association between MVC and maternal mortality (13). Moreover, further associations such as the trigger for immediate delivery or being more likely to die are reported with severe blunt injury (Injury Severity Score (ISS) of 9 or above, or systolic blood pressure (SBP) <90mmHg on arrival) (14). Involvement in MVC is also associated with perinatal mortality (15), injuries to the abdominal region (16), placental abruption secondary to increased intra-abdominal pressure (17), preterm birth, and caesarean section (6). However, more data are required in relation to areas such as fetal outcomes and higher risk pregnancies, particularly regarding sociodemographic characteristics of the mother, specific trimester of pregnancy when exposed to trauma, socioeconomic country conditions, severity and type of trauma, and collision characteristics such as speed. A systematic review on trauma in pregnancy (including five studies reporting complications of involvement in MVC, and fourteen other studies on others form of trauma) showed that MVC and domestic violence were the most common causes of traumatic injury during pregnancy (4). No quality assessment of the included studies was reported in this review. Previous non-systematic reviews have published strategies used to monitor women and fetuses after a crash (18-21). However, to our knowledge there is no systematic review or meta-analysis focused on the maternal and fetal outcomes after MVC in pregnancy.

Review objectives

As the clinical impact on the mother and fetus after MVC has not been well documented, we conducted a systematic review of the effect on maternal and fetal outcomes of MVC in pregnant women, compared to those not involved in a collision.

Methods

We conducted a systematic review and reported it according to recommended standards (22). The review was prospectively registered with PROSPERO (no. CRD42018100788).

Literature search

Searching was from June to August 2018. The following databases were used to identify relevant literature: Medline, Embase, Web of Science, Scopus, LILACS (Latin-American and Caribbean System on Health Sciences Information), Science Citation Index, SciELO (Scientific Electronic Library Online), TRANSPORT, IRRD (International Road Research Documentation), TRANSDOC (European Conference of Ministers of Transportation databases), Cochrane Database of Systematic Reviews (CDSR), and Cochrane Central Register of Controlled Trials (CENTRAL). We also sought to identify unpublished research or research reported in the grey literature by searching a range of relevant databases, including the Inside Conferences, Systems for Information on Grey Literature (SIGLE) and Dissertation Abstracts. Furthermore, the searches of the medical database were supplemented with the Internet search using a general search engine (e.g. Google, www.google.co.uk/) and safetylit.org. Language and date restrictions were not applied to electronic searches. Relevant studies were identified using a combination of, but not limited to, the medical subject headings (MeSH) and keywords for "motor vehicle collision" (OR road traffic collision OR crash OR collision) and "pregnancy" (OR pregnant women OR gravid women OR childbearing women OR maternal).

Review inclusion criteria

Papers were selected if they studied the effects of exposure to trauma due to involvement in an MVC during pregnancy vs. non-exposure, with follow up to verify outcomes in various settings including secondary care, collision and emergency, and inpatient care. Observational studies (cohort studies, case-control design, non-intervention arms of randomised controlled trials) were included. Case series and case reports were excluded. Appendix 1 shows the search strategy for Medline (via Ovid) and Appendix 2 the excluded studies with reasons.

Data extraction and study quality assessment

A double screening of papers was carried out. Two reviewers (CAP & JR) independently extracted the relevant data from each full-text article and data were recorded using a standardized data extraction form. A data extraction form was piloted for each study design and amended as required. Discrepancies were resolved by consensus or by a discussion with a third senior author (ER). We extracted data on a) severe adverse maternal outcomes such as maternal death, miscarriage and preterm birth (<37/40 and <34/40); b) severe adverse fetal outcomes such as intrauterine death/stillbirth and neonatal death. Secondary outcomes were: a) individual components of maternal outcomes such as preterm labour, mode of delivery (vaginal delivery vs caesarean section), premature rupture of membranes (PROM), preterm premature rupture of membranes (PPROM), placental abruption, chorioamnionitis/sepsis and maternal admission to an intensive care unit (ICU) or high dependency unit (HDU); b) individual components of fetal outcomes: respiratory distress syndrome, neonatal ICU admission, low birth weight (LBW) and small for gestational age (SGA).

We also extracted data on 1) adverse outcomes in pregnant women involved in MVC and their offspring in subgroups according to maternal characteristics (low, high and any risk), trimester of exposure, country (low and middle income, high income), type of trauma (penetrating, blunt, burns), severity of trauma (mild, moderate, severe), seatbelt use (yes, no), study quality (low, high); 2) risk factors for pregnancy complications following MVC such as maternal characteristics (age, parity, high risk pregnancy, gestational age), type of trauma, type of motor vehicle, type of collision, collision characteristic (stationary, high or moderate speed) and seat belt use.

The quality assessment of studies was independently evaluated by two reviewers (JR and CAP) using the Newcastle-Ottawa Scale (23). This scale includes 8 items, 4 items about selection criteria of cases or cohorts in case-control or cohort designs, respectively; 2 items about comparability between groups (in both designs); and 3 items about exposure criteria in case-control designs and about outcomes in cohort designs. Any of those studies could be awarded a maximum of one star for each numbered item within the selection and exposure categories. A maximum of two stars could be given for comparability. For the incidence analysis, we considered six aspects (24): 1) representativeness of cohort; 2) design; 3) method of sampling; 4) adequacy of follow-up; 5) if the outcomes were adequately ascertained and 4) if measurement or misclassification bias were minimized. Studies without these features or with unclear reporting were classified to have a high risk of bias.

Patient and Public Involvement

"No patient involved"

Data synthesis

We undertook random-effects meta-analysis to determine the odds ratios (OR) with 95% confidence intervals (CI) for maternal and offspring complications from MVC. We estimated heterogeneity between the included studies with Chi-Square test of Q (I2) excepting when not enough studies were in the meta-analysis (2-3), and we pooled the rates of maternal/fetal complications and reported with 95% CI. For each primary outcome, a meta-analysis was conducted for studies sufficiently homogeneous in terms of the characteristics of participants and exposure. The subgroup analysis was applied in: a) trimester of pregnancy during which the trauma occurred; b) maternal risk status (low, high, any risk); c) type of trauma; d) severity of trauma (using the ISS to categorize the severity of trauma sustained following MVC) (25); e) setting (low and middle income, high-income country); f) year of study publication: (before or after the introduction of mandatory seatbelt legislature in the country of study); and g) study quality according to the Newcastle and Ottawa Scale (23).

Results

Study selection

Out of 1,739 retrieved references, 19 studies met the eligibility criteria (Figure 1). Five of these reported data allowing us to compare pregnancy complications between pregnant women involved in MVC and those not involved in MVC (6, 26-29). The totality of the studies (n = 19) contributed to the analysis of the incidence of pregnancy complications among women involved in MVC (6, 17, 26-42).

Characteristics of included studies

The characteristics of included studies are in Table 1. Included studies were published between 1993 and 2016. Most of them were carried out in developed, high-income countries such as USA (14/18) (26, 28-31, 33-41), Sweden (1/19) (27), Kuwait (1/19) (17) and Israel (1/19) (42). The number of included pregnant women varies, ranging from 39 to 1,094,559. The data was sourced from hospital records/trauma registries (7/19) (17, 31, 32, 35, 38, 39, 42) or from population-level databases (12/19) (6, 26-30, 33, 34, 36, 37, 40, 41). The majority of studies collected information on outcomes of pregnant women involved in MVC during any trimester of pregnancy. 8 out of 19 studies reported information about the use of safety devices such as seatbelts and/or airbag (26, 29, 30, 33, 35, 37-39). Also in eight studies, the authors assessed the severity of MVC injuries with five of these using a validated tool (28, 31, 35, 38, 42) – most of them reporting ISS (28, 31, 35, 42) and one the Revised Trauma Scale (38) .

Quality assessment

60% of studies had a low risk of bias with regards to the adequacy of representativeness and random sample selection (12/19). None of the studies was prospective. The categories of follow up of more than 80% of participants, outcome ascertainment and misclassification bias showed low risk (Figure 2). The five papers included for comparison of complication rates between pregnant women exposed to MVC and those who were not exposed (assessed using the Newcastle-Ottawa Scale) showed generally high quality, with four papers scoring 9/9 (6, 26, 28, 29). The remaining paper scored 8/9, losing one point for the comparability as it did not control for any secondary factors (27).

Incidence of complications among pregnant women involved in motor vehicle crashes

The assessment of adverse outcome incidence among women involved in MVC (using population-level data) demonstrated incidence estimations of 276.43 per 1000 for induction of labour (95% CI 262.54 to 290.54), 191.90 per 1000 for preterm delivery (95% CI 45.98 to 405.74), and 166.65 per 1000 for caesarean section (95% CI 47.34 to 339.00). The estimated incidence rates for other complications included 42.33 per 1000 for PROM, 17.08 per 1000 requiring admission to hospital, 16.14 per 1000 for placental abruption and 15.19 per 1000 for neonatal respiratory distress. A pooled incidence of maternal death was 3.60 per 1000 women (95% CI 0.25 to 10.42, 3 studies, 12,000 women, Tau=1.77). The pooled incidence of perinatal death (fetal death or stillbirth) per 1000 women was 6.60, (95% CI 3.81 to 10.12; 8 studies, 47,992 women; I^2=92.6%) (Table 2). The representation of the maternal and offspring outcomes according to trauma severity are in appendices (Appendices 3 and 4). Using data from single hospital centres, the random pooled estimation for the incidence of admission to hospital was 117.92 per 1000 women (95% CI 109.82 to 126.40) (17, 38); for maternal death was 135.05 per 1000 women (95% CI 131.37 to 138.80) and for fetal death was 5.73 per 1000 women (95% CI 3.05 to 9.77) (Appendices 5 and 6).

Pregnancy complications in women involved vs not involved in motor vehicle crashes

We observed a statistically significant link between involvement in MVC and maternal death (OR 202.3, 95% CI 110.60 to 370.00; single study) (27) (data not shown in table or graphic). Figure 3 shows pooled results from population-level data, demonstrating a positive association between MVC and placental abruption (OR 1.43 95% CI 1.27 to 1.63). Two studies contributed data used in sensitivity analyses stratifying by seatbelt use, where the pooled estimation (26, 29) of fetal death decreased with seatbelt devices, but the association was not statistically significant (OR 0.66 95% CI 0.36 to 1.19) (Figure 1, supplementary). The review manager forest plot displays a positive but not statistically significant association between fetal death and MVC without seatbelt use (OR 5.78 95% CI 0.17 to 201.12, $Tau^2 = 6.51$) (Figure 2, supplementary).

Discussion

Statement of principal findings

This review estimated that for women involved in MVC, maternal death occurrence was 3.6 per 1000 and perinatal death 6.6 per 1000 women. Compared to women not involved in MVC, those involved had an increased odds of placental abruption, antepartum haemorrhage and maternal death. The pooled incidence of complications per 1,000 women involved in MVC was, from the higher incidence to the lower, induction of labour, preterm delivery, caesarean section, premature rupture of membrane, and placental abruption (population level-data).

Strengths and weaknesses of this study

This is the second systematic review, after the one of Mendez Figueroa et al., in 2013 (4), looking at outcomes following MVC in pregnancy. We conducted our review using a prospectively registered protocol (PROSPERO) and reported it in accordance with the international standards (43). This review, to our best knowledge, is the first one examining the link between involvement in MVC, mortality and adverse outcomes that involves evaluation of study quality assessment; 14 studies looking at outcome incidence related to MVC (17, 30-42) and 5 studies comparing outcomes in pregnant women involved in MVC and those who were not (6, 26-29). We used established tools to assess outcome reporting quality for the incidence rates (44) and comparability (45). We included data from population-level and single centre studies, but the analysis and reporting of the results were independent in order to get precision and validity in the estimations. However, a couple of graphics of the maternal and offspring's outcomes incidences have been included as Appendix 3 and 4. Between August 2018 and March 2020, there have been no new studies eligible to include in the systematic review.

For the incidence analysis, we evaluated the quality of the 19 studies of this systematic review. The highest risk was in the design. None of the studies had a prospective design. The representativeness of cohort and the random method of sampling were other limitations of the quality of studies, with 7 out of 19 studies having a high risk of bias in these areas (17, 31, 32, 35, 38, 39, 42). However, the quality assessment of the five papers included for comparison of complication rates between pregnant women involved and not involved in MVC using the Newcastle-Ottawa Scale showed generally high quality, with four papers scoring 9/9 (6, 26, 28, 29).

The weaknesses of this systematic review are as follows. Firstly, outcomes were not reported by trimester, with 13 out of 19 papers focused on MVC at any trimester. Secondly, outcomes, according to seatbelt use, are scarce as only two studies using population-level data looked at safety features as a stratification factor (26, 29). Two studies with data sourced from hospital records/single-site trauma registries (38, 39) and three studies utilising population-level databases (26, 29, 30) reported some outcomes regarding seatbelt-use. Thirdly, we found a limited number of relevant studies comparing outcomes between women involved and not involved in MVC. The majority of the studies were carried out in the USA (26, 28, 29) with most recent one published in 2013 (29). Fourthly, the included studies differed in study design with seven of them using hospital records/single-site trauma registry (17, 31, 32, 35, 38, 39, 42) and twelve population database (6, 26-30, 33, 34, 36, 37, 40, 41). Despite analysing the data within the respective study designs and incorporation of anticipated variation into the statistical model (random-effects) (46), we encountered substantial statistical heterogeneity in the pooled estimates that could not be formally explored due to a limited number of studies and poor reporting of important factors such as trauma severity. As a fifth point, these data apply to developed countries - only one of the papers included data from an underdeveloped country, perhaps influencing the outcomes that might otherwise be seen in the developed world. Finally, in only eight studies did authors assess severity of MVC injuries, with only five of these using a validated tool (28, 31, 35, 38, 42). This was a challenge when aiming to analyse results according to the severity of the crash.

Meaning of the study

The strongest association was found between placental abruption (6, 28, 29) and MVC. Maternal death was associated with involvement in MVC but this finding needs to be treated with caution as the data come from a single study (27). The outcomes in descending order of incidence estimate per 1000 (population-level data) were the induction of labour, preterm delivery, caesarean section, premature rupture of membranes, and admission to hospital, placental abruption and maternal death. In the analyses stratified by use of seatbelt, we observed an association of fetal death with lack of seatbelt use by pregnant women involved in an MVC. However, this finding was not statistically significant and informed by a limited number of studies. Previous studies have shown that pregnant women wearing seatbelt during the MVC did not experience a significantly higher risk of adverse fetal outcomes than women who were not involved in MVC (47) Furthermore, airbags seem to be contributing to the protection of both pregnant drivers and their fetuses (48).

The results of this systematic review provide evidence informing primary prevention measures, recommendations and educational interventions for pregnant women in the context of MVC that should be incorporated into the primary care guidelines.

Unanswered questions and future research

The effects of MVC in pregnant women is a specific field that requires further research and an improved methodological approach to determine the risks of adverse maternal and fetal outcomes.

Additional variables such as trauma severity, the position of the women in the car, use of seatbelt, deployment or non-deployment of an airbag, severity of the crash and gestational week of pregnancy should be recorded in relation to MVC exposure in order to allow more precision when analysing outcomes. A greater number of well-designed studies in a variety of global settings would strengthen current evidence-base.

Conclusions

Pregnant women involved in MVC seem to be at increased risk of maternal death and complications, especially placental abruption, than those not involved in MVC. The risk of complications such as preterm delivery, premature rupture of membranes and caesarean section were also increased. However, these findings need to be treated with caution due to the small number of studies included in the review and considerable differences between studies. Road traffic authorities should be conscious and strict in targeting preventive measures aimed at pregnant users of motor vehicles due to risk associated with potential involvement in MVC.

Word count: 3,147

Author's contribution

PM conducted literature searches and screened publications jointly with JR. CAP and JR extracted the data. CAP and ER drafted the manuscript and conducted the statistical analyses. KSK and ST designed the study review. CAP is the guarantor. Authors VMR, KB, ABC, ST and KSK gave critical revision of the manuscript. All authors had full access to the data and take responsibility for the data analyses. The corresponding author attests that all listed authors meet authorship criteria.

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Data sharing Statement

All data relevant to the study are included in the article or uploaded as supplementary information

Table 1. Characteristics of included studies

Study ID Author, year, Country	Design	Sample size	Time period	Inclusion criteria	Data source	Trimester	Seatbelt use (with data)	Assessment of trauma severity (with data)	Method of assessing trauma severity	Maternal outcomes	Offspring outcomes
Population-level data											
Azar, 2005 USA	population-based matched retrospective cohort *(incidence only)*	5936	2003-2011	Admitted to hospital following MVC while pregnant	Population-based cohort	any	no	no	N/A	Maternal death	------------
Hyde, 2003 USA	retrospective cohort *(incidence and comparison)*	322704	1992-1999	Pregnant drivers involved in MVC	Linked databases (police registry & birth/death certificates)	any	yes	yes	Study-specific definition[1]	------------	Fetal death
Kvarnstrand, 2008 Sweden	retrospective cohort *(incidence and comparison)*	1094559	1991-2001	Maternal inclusion on the accident register > 28 GW	Linked databases (police registry & birth/death certificates)	2nd	no	yes	Study specific definition[2]	Maternal death	Fetal/neonatal death
Kuo, 2007 USA	retrospective chart/database review *(incidence only)*	16982 injuries 4479 (in MVC)	2002	Pregnant women hospitalized with injury (only MVC used)	Sample from population level cohort (National Inpatient Sample)	any	no	no	N/A	Delivery, hospitalization	------------
Schiff, 2005 USA	retrospective cohort *(incidence and comparison)*	17899	1989-2001	Hospitalized for MVC and with a singleton livebirth or fetal death	Linked databases (hospital discharge data & birth/death certificates)	any	no	yes	ISS	Preterm birth, PROM, C-section, placental abruption	Stillbirth LBW, SGA, Fetal distress, RDS, Meconium
Schiff, 2010 USA	retrospective cohort *(incidence only)*	3348	2002-2005	Non-rollover MVC among pregnant front seat occupants	Linked databases (hospital discharge data & birth/death certificates)	any	yes (airbag) no (seatbelt)	no	N/A	Preterm birth, placental abruption, labour induction, C-section	Stillbirth, LBW SGA, RDS Fetal distress Meconium
Vivian-Taylor, 2012 Australia	retrospective cohort *(incidence and comparison)*	604380	2000-2007	Women who gave birth exposed and not exposed to MVC	Linked databases (hospital discharge data & birth/death certificates)	2nd	no	yes	Study-specific definition[3]	Admission, placental abruption, APH, PPH, preterm birth, C-section	Perinatal death (>20th GW), neonatal transfer

Vladutiu, 2013 USA	retrospective cohort *(incidence and comparison)*	878546	2001-2008	Pregnant women 16-46 years, > 20GW, delivering a live/ stillbirth singleton infant	Linked databases (police registry & birth/death certificates)	2nd	yes (seatbelt) yes (airbag)	no	N/A	Placental abruption, PROM, preterm birth	Stillbirth
Weiss, 2002 USA	crash database pregnant vs. non-pregnant (NASS/CDS) *(incidence only)*	32810	1995-1999	Pregnant and non-pregnant women 15–39 years	Sample from population-level database of traffic accidents	any	yes	no	N/A	Maternal death	------------
Weiss, 2008 USA	retrospective cohort *(incidence only)*	1816	1999-2002	Injury-related emergency department visits by pregnant women (only MVC used)	Linked databases (hospital discharge data & birth/death certificates)	any	no	no	N/A	Hospital admission	------------
Whitehead, 2013* USA	PRAMS survey database *(incidence only)*	235329	2000-2005	Survey of women who recently delivered a live-born infant	Population-based cohort (PRAMS)	any	no	no	N/A	Preterm birth, UTI, PROM	------------
Wolf, 1993 USA	population-based retrospective cohort *(incidence only)*	2582	1980-1988	Pregnant women drivers involved in MVC >20GW	Linked databases (police registry & birth/death certificates)	2nd & 3rd	yes	no	N/A	Preterm birth, placental abruption, C-section	Stillbirth, LBW, RDS
Single hospital records/trauma registry											
Aboutanos, 2007 USA	retrospective chart/database review *(incidence only)*	148	2001-2005	Pregnant women presenting to ED following MVC	Single hospital records from trauma centre	any	yes (only in miscarriage)	yes	ISS	Maternal death, miscarriage	Fetal death hydrops fetalis
Baerga-Varela, 2000 USA	retrospective chart/database review *(incidence only)*	39	1986-1996	Admitted to hospital after MVC while pregnant	Single hospital records	any	no	yes	ISS	Maternal death, miscarriage	Stillbirth
Brookfield, 2013 USA	retrospective chart/database review *(incidence only)*	256	1990-2007	Pregnant women presenting to ED following MVC	Single hospital records from trauma centre	any	yes	yes	ISS and RTS	Maternal death, admission to hospital	------------

Chibber, 2015 Kuwait	retrospective chart/database review *(incidence only)*	728	2009-2012	MVC, pregnant, treated at major tertiary hospitals	Single hospital records	2nd	no	no	N/A	Maternal death, placental abruption, preterm birth, uterine rupture, C-Section, admission	Fetal death, fetal distress
Luley, 2013 USA	retrospective chart/database review *(incidence only)*	126	1994-2010	Pregnant women after an MVC >14/40 GA	Single hospital trauma database	2nd & 3rd	yes	no	N/A	Maternal death, placental abruption, C-section	Stillbirth
Miller, 2016 Israel	retrospective cohort *(incidence only)*	3794	2006-2013	Women 18-40 years, in MVC and hospitalized (only pregnant cohort used)	National trauma registry	any	no	no	ISS	Maternal death, miscarriage, placental abruption, C-section	Stillbirth
Orji, 2002 Nigeria	retrospective chart/database review *(incidence only)*	84	1980-2000	Pregnant women in MVC managed in tertiary hospitals	Single hospital records**	any	no	no	N/A	Maternal death, placental abruption, uterine rupture, C-section	Perinatal death (fetal death), fetal tachycardia

*ISS: Injury Severity Score; RTS: Revised Trauma Score; ICU: Intensive Care Unit, N/A not applicable; GA: Gestational Age; LBW: Low birth weight; SGA: Small for gestational age; RDS: Respiratory distress syndrome. *National survey; **Two hospitals in same region included; [1]Possible/probable/incapacitated/fatal; [2]Fatal/major/minor/uninjured; [3]'Severe' = admission to ICU and/or blood transfusion and/or injury to abdomen/pelvis/lower back.*

Table 2. Incidence of adverse outcomes per 1,000 women involved in motor vehicle crashes.

Outcome and study	Number of studies	Number of women	Incidence estimate per 1,000 women	95% CI
Maternal				
Maternal death	**3**	**12000**	**3.60**	**(0.25 to 10.42)**
Azar, 2005			6.57	(4.68 to 8.97)
Kvarnstrand, 2008			6.61	(3.70 to 10.88)
Miller, 2016			0.26	(0.01 to 1.47)
Admission to hospital	**2**	**3838**	**17.08**	**(13.20 to 21.46)**
Vivian-Taylor, 2012			8.90	(5.28 to 14.03)
Weiss, 2008			29.19	(21.94 to 38.0)
Placenta abruption	**6**	**36737**	**16.14**	**(7.04 to 28.78)**
Wolf, 1993			8.10	(5.02 to 12.36)
Miller, 2016			1.05	(0.29 to 2.70)
Schiff, 2005			113.40	(88.80 to 142.01)
Schiff, 2010			12.25	(8.80 to 16.58)
Vivian-Taylor, 2012			16.32	(11.26 to 22.84)
Vladutiu, 2013			7.17	(6.15 to 8.31)
Preterm delivery	**5**	**265680**	**191.90**	**(45.98 to 405.74)**
Schiff, 2005			316.15	(278.53 to 355.65)
Schiff, 2010			97.37	(87.53 to 107.92)
Vivian-Taylor, 2012			83.09	(71.42 to 95.98)
Vladutiu, 2013			110.33	(106.43 to 114.33)
Whitehead, 2013			437.00	(435.00 to 439.01)
PROM	**3**	**260310**	**42.33**	**(5.87 to 109.24)**
Schiff, 2005			22.34	(11.95 to 37.89)
Vladutiu, 2013			23.53	(21.66 to 25.51)
Whitehead, 2013			96.00	(94.81 to 97.20)
Labour induction	**2**	**3930**	**276.43**	**(262.54 to 290.54)**

Schiff, 2005			223.37	(190.15 to 259.42)
Schiff, 2010			286.14	(270.87 to 301.78)
Caesarean section	**5**	**12338**	**166.65**	**(47.34 to 339.00)**
Miller, 2016			6.06	(3.85 to 9.08)
Schiff, 2005			254.30	(219.38 to 291.73)
Schiff, 2010			259.26	(244.48 to 274.46)
Vivian-Taylor, 2012			260.14	(241.13 to 279.85)
Wolf, 1993			171.68	(157.35 to 186.76)
Offspring				
Perinatal death	**8**	**47992**	**6.60**	**(3.81 to 10.12)**
Kvarnstrand, 2008	fetal/neonatal		17.62	(12.62 to 23.92)
Hyde, 2003	fetal		5.01	(3.66 to 6.70)
Miller, 2016	stillbirth		0.79	(0.16 to 2.31)
Schiff, 2005	fetal		12.03	(4.85 to 24.62)
Vivian-Taylor, 2012	stillbirth		16.82	(11.67 to 23.42)
Vladutiu, 2013	stillbirth		5.25	(4.38 to 6.23)
Schiff, 2010	fetal		4.18	(2.29 to 7.01)
Wolf, 1993	fetal		3.47	(1.59 to 6.58)
Fetal distress	**2**	**3930**	**60.09**	**(52.85 to 67.77)**
Schiff, 2005			132.30	(105.84 to 162.56)
Schiff, 2010			50.48	(43.31 to 58.44)
Meconium at delivery	**2**	**3930**	**52.61**	**(45.82 to 59.85)**
Schiff, 2005			63.57	(45.15 to 86.57)
Schiff, 2010			51.08	(43.86 to 59.08)
RDS	**3**	**6522**	**15.19**	**(5.83 to 28.68)**
Schiff, 2005			32.65	(19.77 to 50.51)
Schiff, 2010			14.64	(10.85 to 19.30)
Wolf, 1993			6.17	(3.53 to 10.00)

***Data source: population database**; CI, Confidence Interval; PROM: Premature Rupture of Membranes; RDS: Respiratory Distress Syndrome.*

Figures

Figure 1. The study selection process in the systematic review of outcomes on pregnant women involved in motor vehicle crashes

Figure 2. The quality assessment of the included studies

Figure 3. Comparison of outcomes between women involved and not involved in motor vehicle crashes

Figure 1. (Supplementary). Comparison of pregnancy complications between women involved and not involved in motor vehicle crashes stratified by seatbelt use

Figure 2. (Supplementary). Comparison of fetal death between women involved and not involved in motor vehicle crashes stratified by seatbelt use

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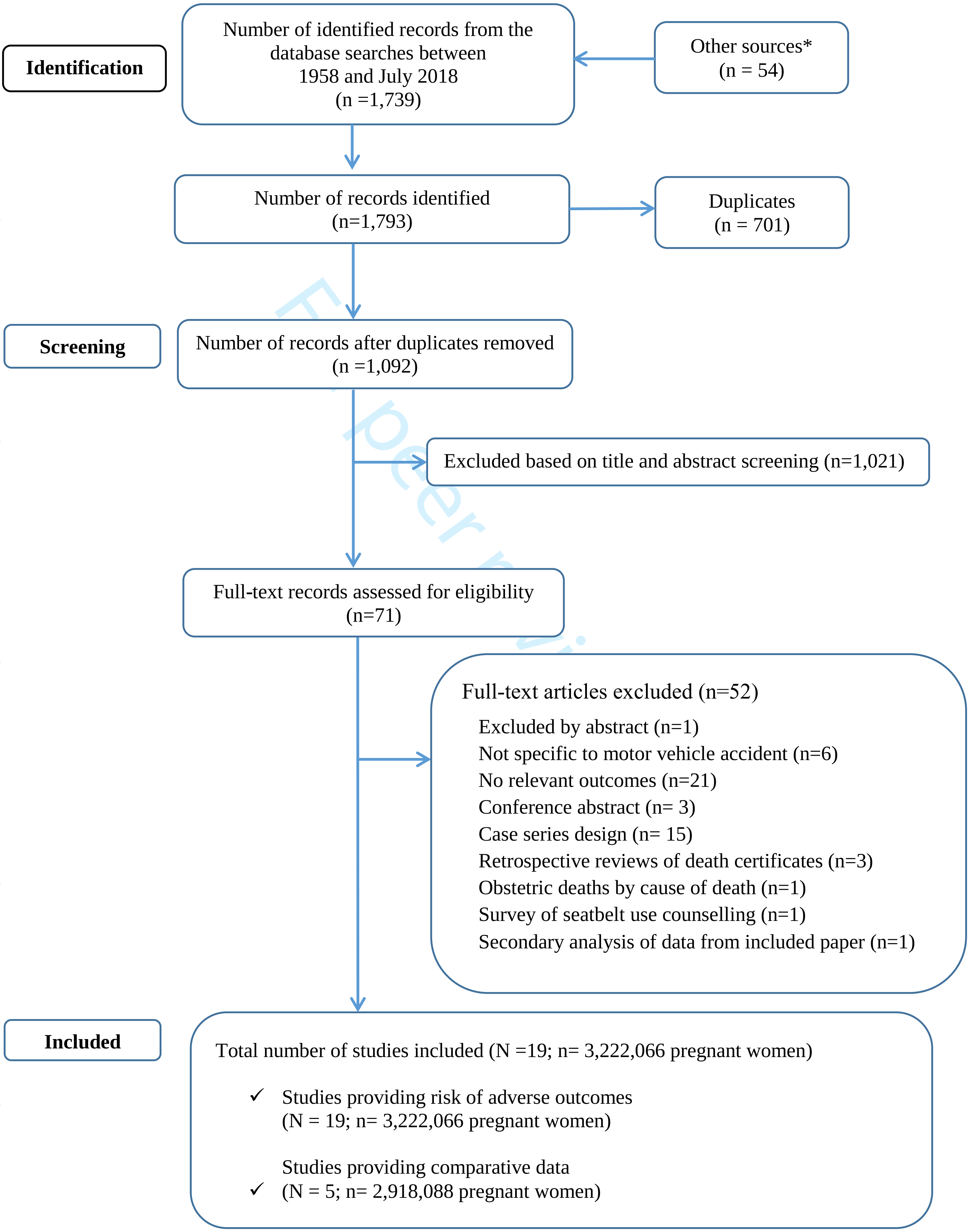
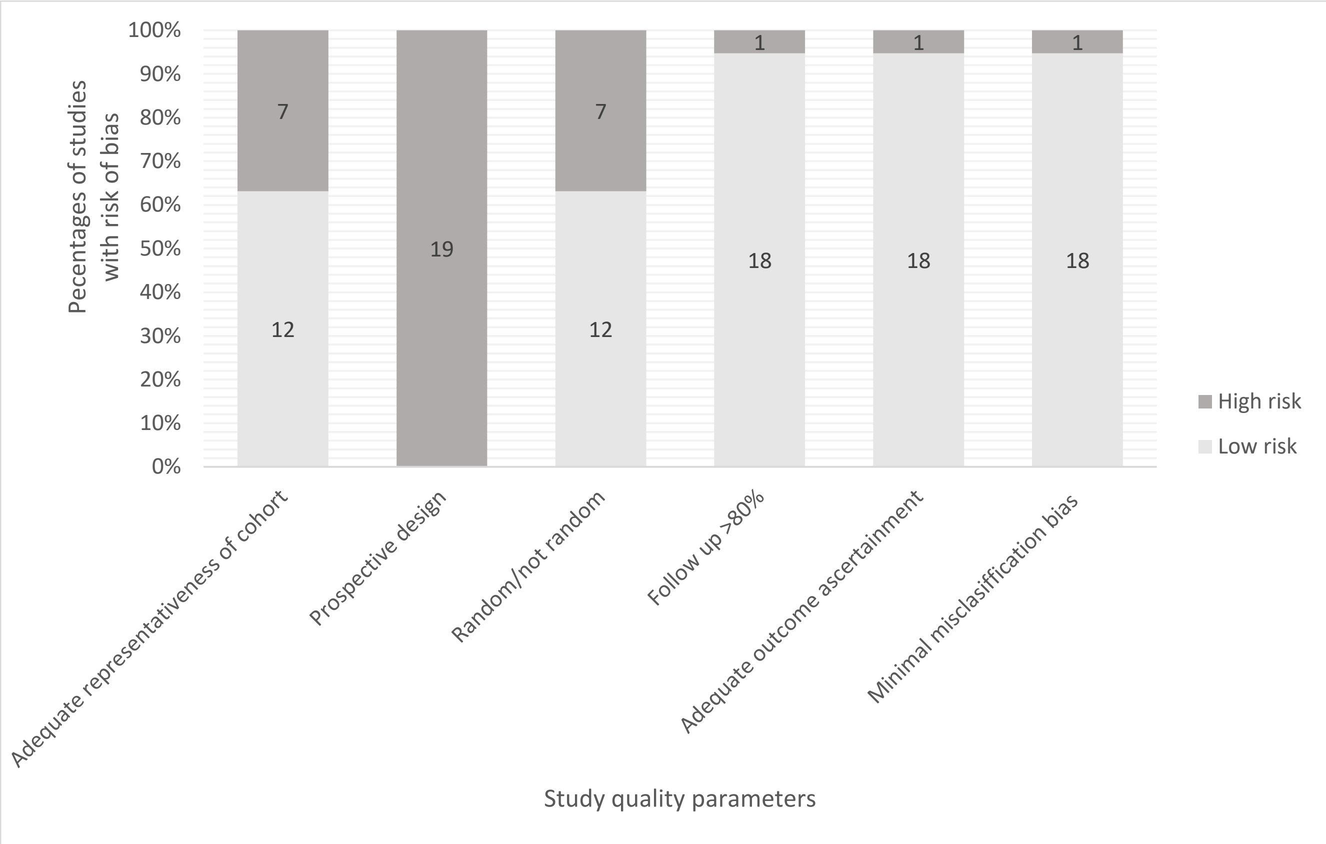


**references of relevant non-systematic reviews and Google scholar*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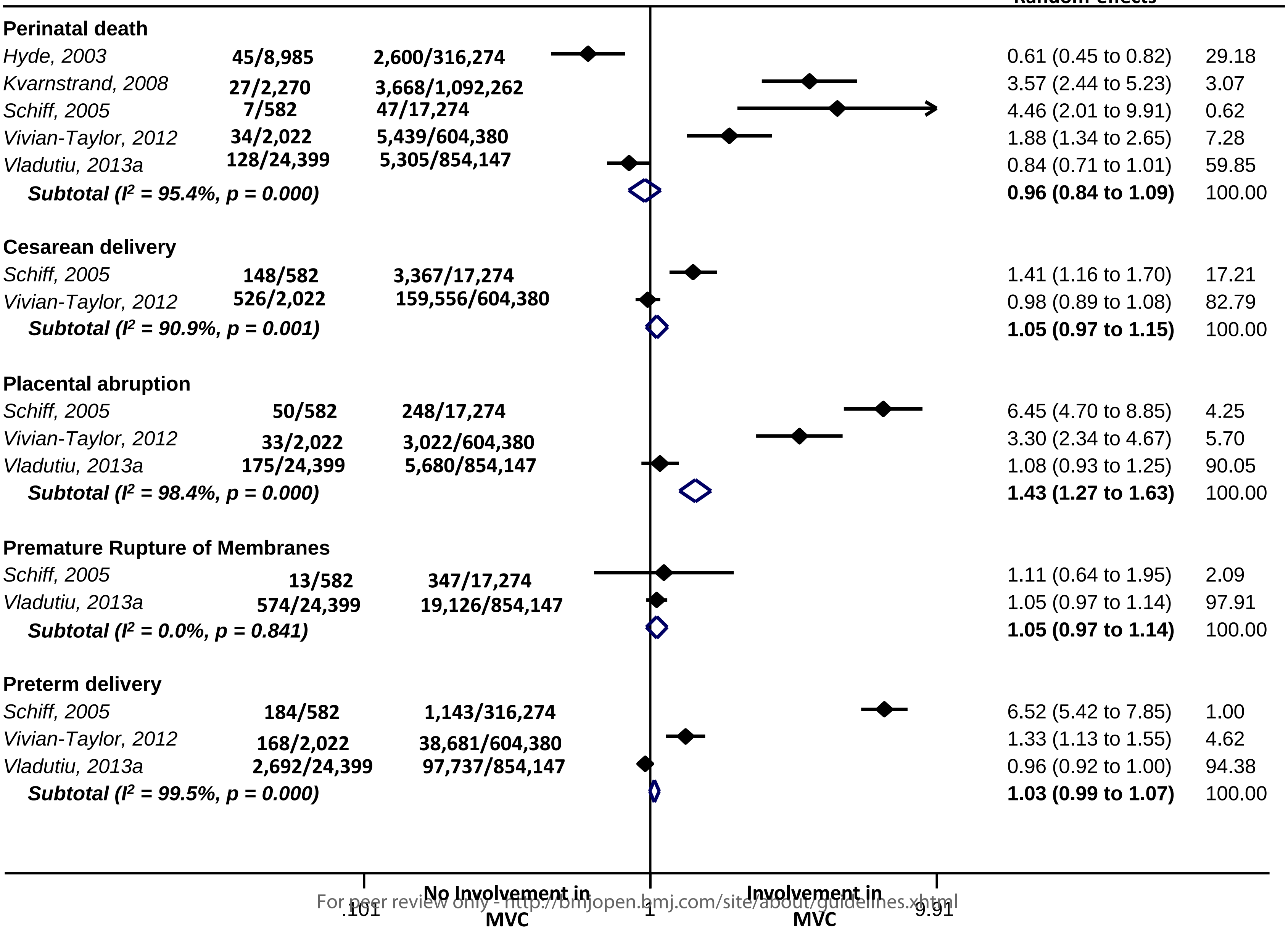
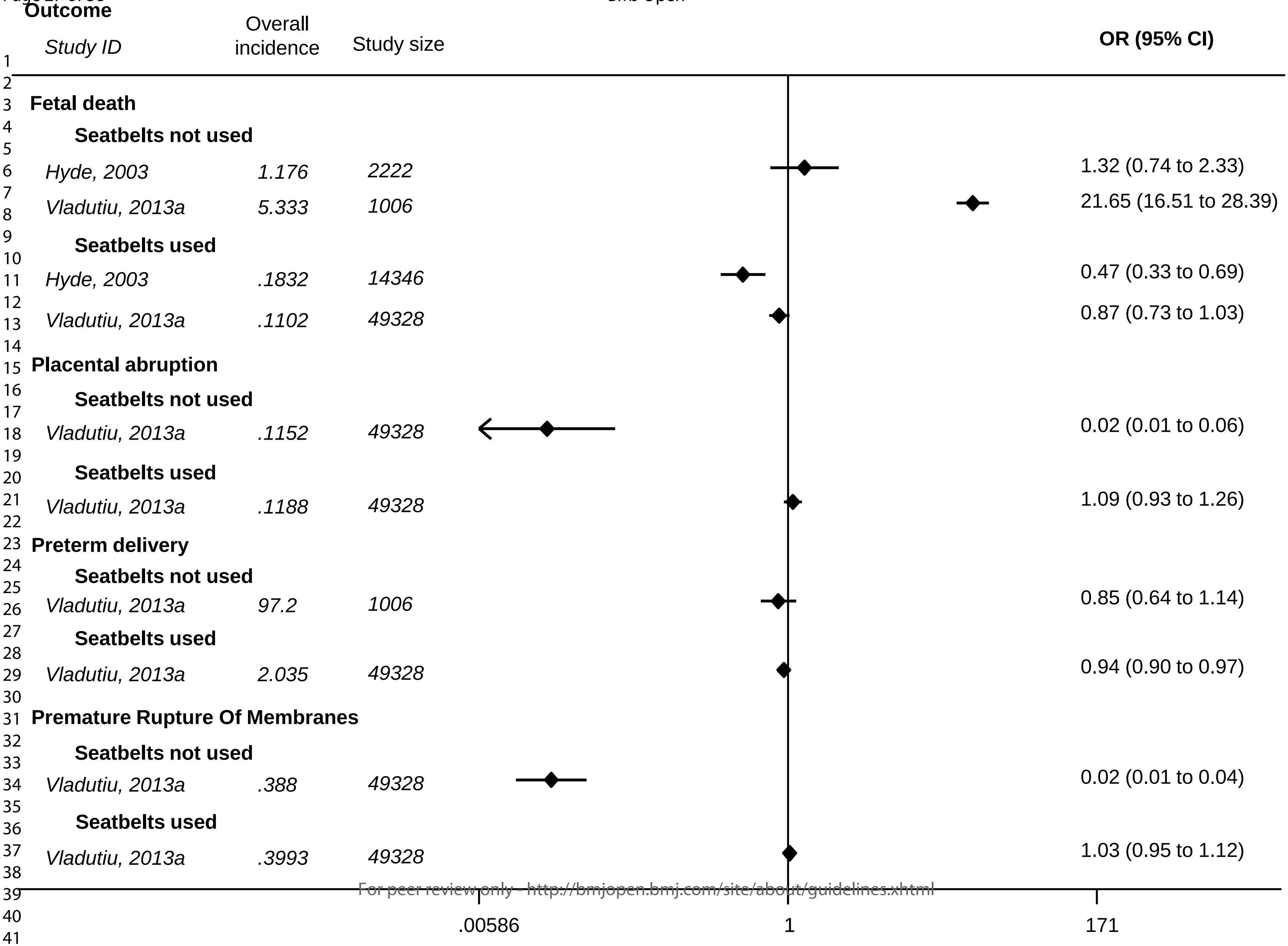
High risk
Low risk
Adequate representativeness of cohort
Prospective design
Random/not random
Follow up >80%
Adequate outcome ascertainment
Minimal misclasiffication bias
Study quality parameters

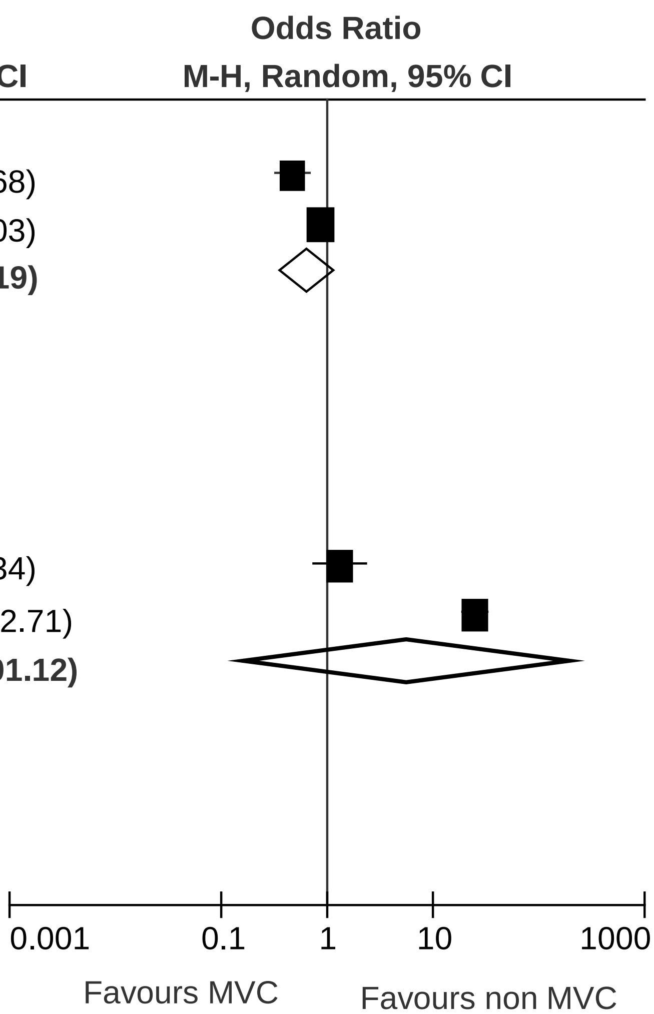
Outcome Study ID	Events/exposed	Events/non-exposed	OR (95% CI) Random-effects	Weight %
Perinatal death				
Hyde, 2003	45/8,985	2,600/316,274	0.61 (0.45 to 0.82)	29.18
Kvarnstrand, 2008	27/2,270	3,668/1,092,262	3.57 (2.44 to 5.23)	3.07
Schiff, 2005	7/582	47/17,274	4.46 (2.01 to 9.91)	0.62
Vivian-Taylor, 2012	34/2,022	5,439/604,380	1.88 (1.34 to 2.65)	7.28
Vladutiu, 2013a	128/24,399	5,305/854,147	0.84 (0.71 to 1.01)	59.85
Subtotal (I^2 = 95.4%, p = 0.000)			**0.96 (0.84 to 1.09)**	100.00
Cesarean delivery				
Schiff, 2005	148/582	3,367/17,274	1.41 (1.16 to 1.70)	17.21
Vivian-Taylor, 2012	526/2,022	159,556/604,380	0.98 (0.89 to 1.08)	82.79
Subtotal (I^2 = 90.9%, p = 0.001)			**1.05 (0.97 to 1.15)**	100.00
Placental abruption				
Schiff, 2005	50/582	248/17,274	6.45 (4.70 to 8.85)	4.25
Vivian-Taylor, 2012	33/2,022	3,022/604,380	3.30 (2.34 to 4.67)	5.70
Vladutiu, 2013a	175/24,399	5,680/854,147	1.08 (0.93 to 1.25)	90.05
Subtotal (I^2 = 98.4%, p = 0.000)			**1.43 (1.27 to 1.63)**	100.00
Premature Rupture of Membranes				
Schiff, 2005	13/582	347/17,274	1.11 (0.64 to 1.95)	2.09
Vladutiu, 2013a	574/24,399	19,126/854,147	1.05 (0.97 to 1.14)	97.91
Subtotal (I^2 = 0.0%, p = 0.841)			**1.05 (0.97 to 1.14)**	100.00
Preterm delivery				
Schiff, 2005	184/582	1,143/316,274	6.52 (5.42 to 7.85)	1.00
Vivian-Taylor, 2012	168/2,022	38,681/604,380	1.33 (1.13 to 1.55)	4.62
Vladutiu, 2013a	2,692/24,399	97,737/854,147	0.96 (0.92 to 1.00)	94.38
Subtotal (I^2 = 99.5%, p = 0.000)			**1.03 (0.99 to 1.07)**	100.00




Outcome
Study ID
Overall incidence
Study size
OR (95% CI)
Fetal death
Seatbelts not used
Hyde, 2003 1.176 2222 1.32 (0.74 to 2.33)
Vladutiu, 2013a 5.333 1006 21.65 (16.51 to 28.39)
Seatbelts used
Hyde, 2003 .1832 14346 0.47 (0.33 to 0.69)
Vladutiu, 2013a .1102 49328 0.87 (0.73 to 1.03)
Placental abruption
Seatbelts not used
Vladutiu, 2013a .1152 49328 0.02 (0.01 to 0.06)
Seatbelts used
Vladutiu, 2013a .1188 49328 1.09 (0.93 to 1.26)
Preterm delivery
Seatbelts not used
Vladutiu, 2013a 97.2 1006 0.85 (0.64 to 1.14)
Seatbelts used
Vladutiu, 2013a 2.035 49328 0.94 (0.90 to 0.97)
Premature Rupture Of Membranes
Seatbelts not used
Vladutiu, 2013a .388 49328 0.02 (0.01 to 0.04)
Seatbelts used
Vladutiu, 2013a .3993 49328 1.03 (0.95 to 1.12)
.00586
1
171

Study ID (Subgroup)	MVC Events	MVC Total	Non MVC Events	Non MVC Total	Weight	Odds Ratio M-H, Random, 95% CI
Fetal deaths (seatbelts used)						
Hyde 2003	28	7145	2600	313674	46.2%	0.47 (0.32 to 0.68)
Vladutiu 2013	133	24531	5305	848073	53.8%	0.87 (0.73 to 1.03)
Subtotal (95% CI)		**31676**		**1161747**	**100.0%**	**0.65 (0.36 to 1.19)**
Total events	**161**		**7905**			
Heterogeneity: $Tau^2 = 0.17$; $Chi^2 = 8.58$, df = 1 (P = 0.003); $I^2 = 88\%$						
Test for overall effect: Z = 1.39 (P = 0.16)						
Fetal death (seatbelts not used)						
Hyde 2003	12	1099	2600	313674	49.8%	1.32 (0.75 to 2.34)
Vladutiu 2013	60	443	5305	848073	50.2%	24.89 (18.93 to 32.71)
Subtotal (95% CI)		**1542**		**1161747**	**100.0%**	**5.78 (0.17 to 201.12)**
Total events	**72**		**7905**			
Heterogeneity: $Tau^2 = 6.51$; $Chi^2 = 126.07$, df = 1 (P < 0.00001); $I^2 = 99\%$						
Test for overall effect: Z = 0.97 (P = 0.33)						

Test for subgroup differences: $Chi^2 = 1.41$, df = 1 (P = 0.24), $I^2 = 28.9\%$



*MVC, motor vehicle crash

Appendix 1. Search strategy for MEDLINE (via Ovid) executed from database inception up to July 2018

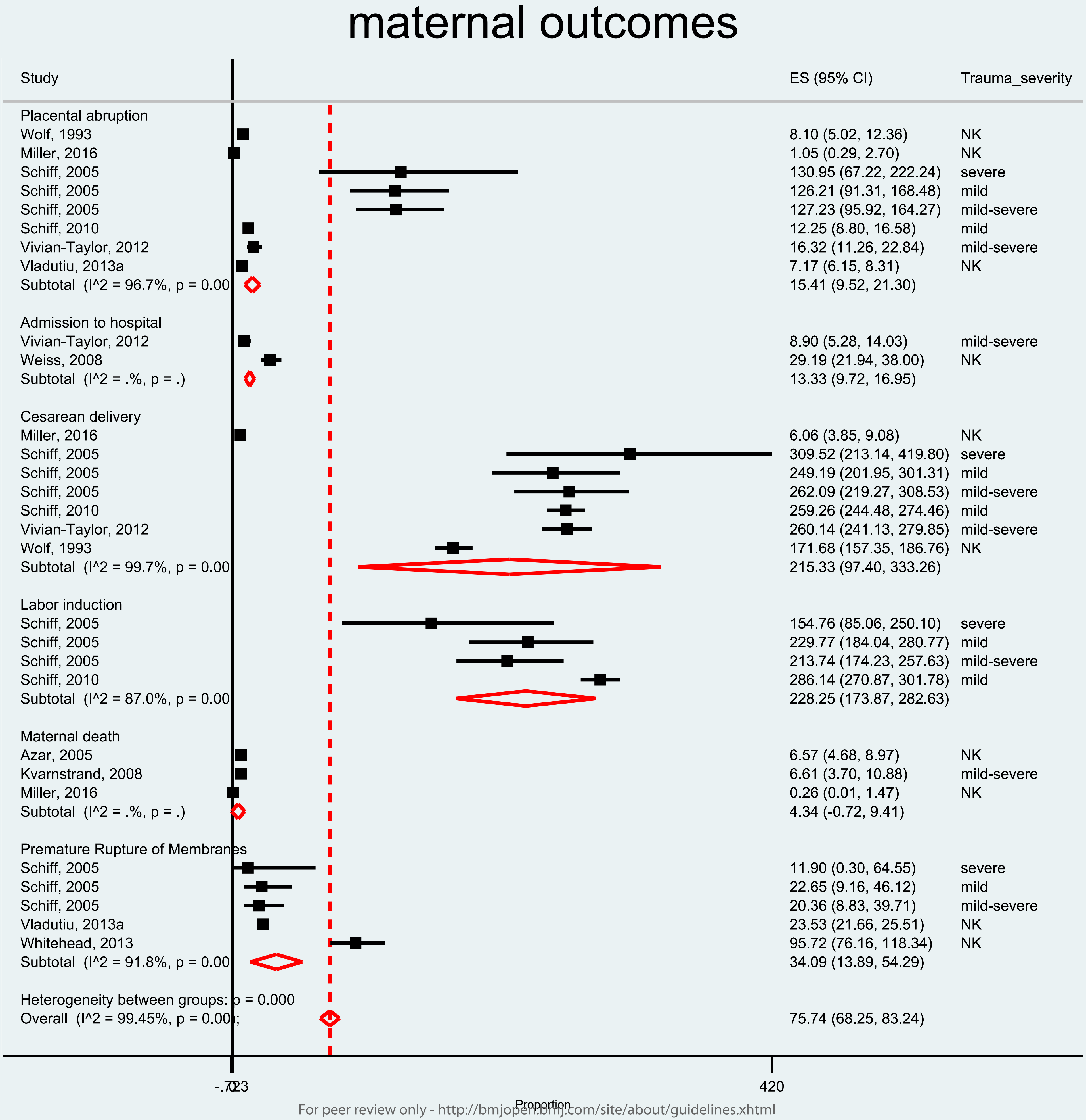
Item	Search term
1	pregnancy.af.
2	pregnan*.sh.
3	gravidity.sh.
4	gravid*.sh.
5	gestation*.sh.
6	pregnant women.sh.
7	pregnant wom#n.sh.
8	(child adj3 bearing).tw.
9	childbearing.af.
10	matern*.sh.
11	vehicle* crash*.af.
12	vehicle* accident*.af.
13	vehicle* collision*.af.
14	motor vehicle crash*.af.
15	motor vehicle accident*.af.
16	motor vehicle collision*.af.
17	motor vehicle injur*.af.
18	vehicle* injur*.af.
19	road traffic crash*.af.
20	road traffic accident*.af.
21	road traffic collision*.af.
22	road traffic injur*.af.
23	auto* crash*.af.
24	auto* accident*.af.
25	auto* collision*.af.
26	auto* injur*.af.
27	car crash*.af.
28	car accident*.af.
29	car collision*.af.
30	car injur*.af.
31	(car adj3 trauma).af.
32	(automobile adj3 trauma).af.
33	(automotive adj3 trauma).af.
34	(road traffic adj3 trauma).af.
35	(motor vehicle adj3 trauma).af.
36	1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10
37	11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34 or 35
38	36 and 37

Appendix 2 List of excluded studies with reasons

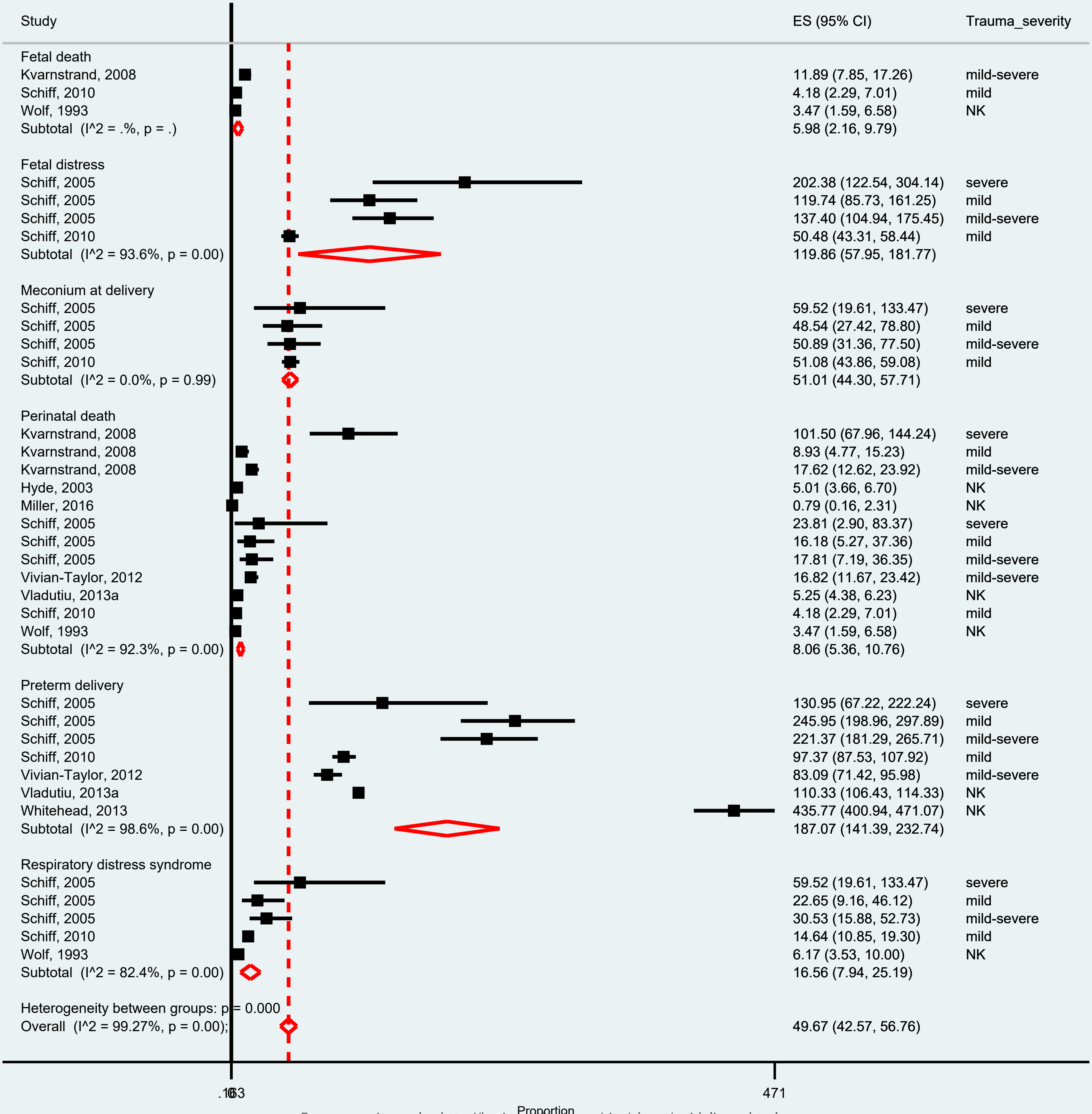
Study ID	Reason	Reference
Al Mulhim, 2012	Pregnancy loss or not after trauma in Arabic pregnant women	*EMHJ. Vol. 18 No. 5 2012*
Battaloglu 2016	From a cohort of 15,140 female patients, 173 were pregnant women in the trauma registry. 55.5% of them from vehicle collision	**SR Petrone, 2017** *Injury, Int. J. Care Injured 47 (2016) 184-187*
Barre 2006	Pregnant women with abdominal trauma during pregnancy (n=65). Half of them from a traffic accident.	**SR Petrone, 2017** *La Revue Sage-Femme. Vol 5, Issue 6, 2006, 312-316*
Cannada 2010	Pregnant women with orthopaedic injuries (n=65)	**SR Petrone, 2017** *Injury, Infection, and Critical Care.2010. Vol. 69 (3)*
Chamberlain, 2011	Communication abstract. Retrospective cohort study. Identification of 272 pregnant trauma victims. 78.6% of them incurred in a MVC. No data to extract	*American Journal of Obstetrics & Gynecology Supplement to January 2011*
Cheng, 2012	Maternal complications during delivery according to uninjured, minor and severe injuries. 2,881 pregnant women (47,4%) involved in MVC	*World J Surg (2012) 36:2767–2775*
Connolly, 1997	476 maternal records of trauma cases. 54.6% were MVC. No more data available	*American Journal of Perinatology.1997.Vol. 14 (6)*
Corsi 1999	Twenty-seven traumatised pregnant women were analysed retrospectively over a period of 9 years in Sao Paulo, Brazil	**SR Petrone, 2017** *Injury, Int. J. Care Injured 30 (1999) 239-243*
Dannenberg, 1995	Homicide and other injuries as causes of maternal death between 1987 and 1991 in New York	*Am J Obstet Gynecol Vol.172 (5)*
Deshpande, 2017	Trauma impact on maternal mortality. Comparability between pregnant vs. non pregnant women	*American Journal of Obstetrics & Gynecology 2017. 590.e2*
El Kady 2004	Retrospective cohort study of women hospitalized for Trauma in California	**SR Petrone, 2017** *American Journal of Obstetrics and Gynecology (2004) 190, 1661-8*
El Kady D, 2006	Fractures injuries on maternal/neonatal outcomes in United States	**SR Méndez -Figueroa 2013** *American Journal of Obstetrics and Gynecology (2006) 195, 711–6*
Fischer 2011	Minor trauma and poor fetal outcomes in Tennessee, Memphis	**SR Petrone, 2017** *Injury, Infection, and Critical Care. 2011. Vol. 71 (1)*
Gibbins, 2017	Communication. MVC and Stillbirth. Secondary analysis of 439 stillbirth	American Journal of Obstetrics & Gynecology Supplement to January 2017
Goodwin, 1990	Case-series of trauma pregnant women between 1987 and 1988 in Los Angeles	**SR Méndez -Figueroa 2013** *Am J Obstet Gynecol. 1990 Vol. 162 (3).*
Hardt, 2013	Prenatal risk screening to identify women at increased risk for traumatic pregnancy-	*Women's Health Issues 23-3 (2013) e187–e193*

	associated death	
Hardy, 1974	Maternal mortality ratios at large urban charity hospitals from 1941 to 1971	*Obstetric and Gynecology. 1974. Vol.43 (1)*
Harland 2014	Risks factors of maternal injuries in a population-based sample of pregnant women from Iowa	**SR Petrone, 2017** *Journal of Women's Health. 2014. Vol. 23 (12)*
Hitosugi 2006	135 traffic accidents involving Japanese pregnant women from insurance companies. The outcomes of neonates determined by their condition 1 month after birth (death/abortion/healthy)	**SR Petrone, 2017** *Forensic Science International 159 (2006) 51-54*
Ikossi, 2005	Risks factors of trauma in pregnant women from San Francisco, California	*J Am Coll Surg. Vol. 2005. 200 (1)*
Lynch, 2011	Pregnancy associated- death in Ohio: 2003-2007	American Journal of Obstetrics & Gynecology Supplement to January 2011
Manoogian, 2015	Injuries characteristics between pregnant vs non pregnant women occupants (not outcome)	*Accident Analysis and Prevention 74 (2015). 69–76*
Melamed 2012	Outcomes following blunt trauma in Pregnant women from Israel	**SR Petrone, 2017** *The Journal of Maternal-Fetal and Neonatal Medicine. 2012; 25(9): 1612–1617*
Mesdaghinia, 2012	Causes of trauma in 32 pregnant women with trauma in a Hospital in Iran	*Arch Trauma Res. 2012;1(1):23-26*
Nannini, 2008	Risks of injury in pregnant women in Massachusets	*Journal of Midwifery & Women's Health.2008. Vol.53 (1)*
Omoke, 2013	Trauma during pregnancy in a Nigerian setting	*Int J Crit Illn Inj Sci. 2013; 3(4): 269–273.*
Osei-Ampofo, 2016	A cross-sectional study with 134 pregnant women from Ghana visiting the emergency care. Leading injury MVC (23%). Not outcomes	*African Journal of Emergency Medicine (2016) 6, 87 –93*
Pak, 1998	Delivery outcomes after a blunt abdominal trauma in 85 pregnant women	*Am J Obstet Gynecol. 1998. Vol. 179 (5)*
Patteson, 2007	High risk factors involved in trauma during pregnancy. Not outcomes	*The Journal of TRAUMA Injury, Infection, and Critical Care. 2007. Vol 62 (4)*
Pearlman, 1990	Not possible to assess full text	SR Méndez -Figueroa 2013
Schiff, 1997	Seat Bealt use. Protective factor of maternal mortality after a MVC in Mexico	*WJM, 1997. Vol. 167 (1)*
Schuster, 2016	Communication abstract. Impact of blunt trauma on maternal and pregnancy outcome. MVC the most common injury mechanism (70%). Pennsylvania Trauma Systems Foundation Database (1996-2013).	*American Journal of Obstetrics & Gynecology. Supplement to January 2016*
Schuster, 2018	Pennsylvania Trauma Systems Foundation Database. ISS>9 and SBP<90mmHg are predictors for poor outcomes after trauma during pregnancy	*Trauma, 2018. Vol. 20(1) 30–37*
Sela, 2011	Treatment provided to pregnant motor vehicle accident (MVA) casualties in a mature trauma system in Israel	*Annals of Surgery, 2011.Vol.254 (2)*

Shah, 1998	Trauma in general in pregnant women	*J Trauma. 1998 Jul;45(1):83-6*
Shakerian 2015	Determining adherence to recommended imaging guidelines in pregnant women from Victoria, Australia	**SR Petrone, 2017** *J Trauma Acute Care Surg. 2015.Vol. 78 (1)*
Shiff 2002	Retrospective cohort study to assess outcomes of pregnant women hospitalized for injury in Washington State from 1989 to 1997	**SR Petrone, 2017** *J Trauma. 2002; 53: 939–945.*
Sirin, 2007	Report the prevalence of seatbelt counselling by prenatal care providers during pregnancy in USA	*Matern Child Health J (2007) 11:505–510*
Tinker 2010	Risks factors involved in injuries in pregnant women from the National Birth Defects Prevention Study, USA	**SR Petrone, 2017** *Journal of Women's Health. 2010. Vol. 19 (2)*
Van der Knoop, 2015	Effect of maternal trauma in fetal motility at term and at one year of age	*Early Human Development 91 (2015) 511–517*
Van der Knoop, 2018	Matched case-control study. Neurobehavioral outcome in 6-18 year old children after trauma in pregnancy	*European Journal of Paediatric Neurology (2018), 22(5):845-853*
Vladutiu, 2013b	Same sample Vladutiu 2013a; excluded as a secondary analysis from already included study	*Accid Anal Prev. 2013; 55: 165–171*
Wahabi, 2007	45 MVC case series pregnant women collected over a 10- year period	*Saudi Med J. 2007. Vol. 28 (9)*
Wall 2014	Pregnant trauma patiens from South Africa (mainly assaults)	**SR Petrone, 2017** *Injury, Int. J. Care Injured 45 (2014) 1220–1223*
Weiner 2016	Minor trauma during pregnancy, not associated with adverse pregnancy outcomes, Israel	**SR Petrone, 2017** *European Journal Of Obstetrics & Gynecology and Reproductive Biology 203 (2016): 78–81*
Weiss, 1999	Retrospect review of death certificates	*43rd Annual Proceedings Association for the Advancement of Automotive Medicine September 20-21, 1999. Barcelona (Sitges), Spain*
Weiss, 2001	Retrospect review of death certificates	*JAMA, 2001. Vol. 286 (15)*
Weiss, 2002a	N/A	
Zangene, 2015	102 cases of trauma in pregnancy registered in Iran from 2007 to 2010. MVC the most frequent (45%)	*Global Journal of Health Science. 2015. Vol 7 (2)*


maternal outcomes
Study
ES (95% CI)
Trauma_severity
Placental abruption
Wolf, 1993 | 8.10 (5.02, 12.36) | NK
Miller, 2016 | 1.05 (0.29, 2.70) | NK
Schiff, 2005 | 130.95 (67.22, 222.24) | severe
Schiff, 2005 | 126.21 (91.31, 168.48) | mild
Schiff, 2005 | 127.23 (95.92, 164.27) | mild-severe
Schiff, 2010 | 12.25 (8.80, 16.58) | mild
Vivian-Taylor, 2012 | 16.32 (11.26, 22.84) | mild-severe
Vladutiu, 2013a | 7.17 (6.15, 8.31) | NK
Subtotal (I^2 = 96.7%, p = 0.00 | 15.41 (9.52, 21.30)
Admission to hospital
Vivian-Taylor, 2012 | 8.90 (5.28, 14.03) | mild-severe
Weiss, 2008 | 29.19 (21.94, 38.00) | NK
Subtotal (I^2 = .%, p = .) | 13.33 (9.72, 16.95)
Cesarean delivery
Miller, 2016 | 6.06 (3.85, 9.08) | NK
Schiff, 2005 | 309.52 (213.14, 419.80) | severe
Schiff, 2005 | 249.19 (201.95, 301.31) | mild
Schiff, 2005 | 262.09 (219.27, 308.53) | mild-severe
Schiff, 2010 | 259.26 (244.48, 274.46) | mild
Vivian-Taylor, 2012 | 260.14 (241.13, 279.85) | mild-severe
Wolf, 1993 | 171.68 (157.35, 186.76) | NK
Subtotal (I^2 = 99.7%, p = 0.00 | 215.33 (97.40, 333.26)
Labor induction
Schiff, 2005 | 154.76 (85.06, 250.10) | severe
Schiff, 2005 | 229.77 (184.04, 280.77) | mild
Schiff, 2005 | 213.74 (174.23, 257.63) | mild-severe
Schiff, 2010 | 286.14 (270.87, 301.78) | mild
Subtotal (I^2 = 87.0%, p = 0.00 | 228.25 (173.87, 282.63)
Maternal death
Azar, 2005 | 6.57 (4.68, 8.97) | NK
Kvarnstrand, 2008 | 6.61 (3.70, 10.88) | mild-severe
Miller, 2016 | 0.26 (0.01, 1.47) | NK
Subtotal (I^2 = .%, p = .) | 4.34 (-0.72, 9.41)
Premature Rupture of Membranes
Schiff, 2005 | 11.90 (0.30, 64.55) | severe
Schiff, 2005 | 22.65 (9.16, 46.12) | mild
Schiff, 2005 | 20.36 (8.83, 39.71) | mild-severe
Vladutiu, 2013a | 23.53 (21.66, 25.51) | NK
Whitehead, 2013 | 95.72 (76.16, 118.34) | NK
Subtotal (I^2 = 91.8%, p = 0.00 | 34.09 (13.89, 54.29)
Heterogeneity between groups: p = 0.000
Overall (I^2 = 99.45%, p = 0.00); | 75.74 (68.25, 83.24)
420
Proportion

offspring outcomes



Appendix 5. Incidence of maternal, fetal & neonatal complications from single studies

Outcome	Total sample size	Incidence estimate per 1,000 women (95%CI)
Maternal outcomes		
Placental problems	235329	100.00 (98.79, 101.22)
Miscarriage	3794	1.85 (0.74, 3.80)
Antepartum haemorrhage	2022	47.48 (38.62, 57.67)
Postpartum haemorrhage	2022	77.65 (66.35, 90.18)
Vaginal bleeding	235329	247.00 (245.26, 248.75)
Hospital stay >=6 days	5936	117.92 (109.82, 126.40)
Maternal death or hospitalisation	32810	135.05 (131.37, 138.80)
Fetal and neonatal		
Hypoxia	582	22.34 (11.95, 37.89)
Neonatal death	2270	5.73 (3.05, 9.77)
Neonatal transfer	2022	42.53 (34.16, 52.26

Appendix 6. Incidence in non-population level data

Outcome	Study ID	Number of events	Group size	Trauma severity level
Admission to hospital	Brookfield, 2013	182	256	Not given
	Chibber, 2015	648	728	Not given
Caesarean delivery	Chibber, 2015	529	728	Not given
	Luley 2013	32	126	Not given
	Orji, 2002	2	84	Not given
Fetal death	Aboutanos, 2007	1	148	Not given
	Chibber, 2015	78	728	Not given
Fetal distress	Chibber, 2015	412	728	Not given
Fetal tachycardia	Orji, 2002	10	84	Not given
Hydrops fetalis	Aboutanos, 2007	1	148	Not given
Maternal death	Aboutanos, 2007	0	148	Not given
	Baerga-Varela, 2000	1	39	Severe
	Brookfield, 2013	7	256	Not given
	Chibber, 2015	100	728	Not given
Maternal death	Orji, 2002	2	84	Not given
Miscarriage	Aboutanos, 2007	5	148	Not given
	Baerga-Varela, 2000	7	39	Mild to severe
Perinatal death	Baerga-Varela, 2000	23	39	Mild to severe
	Luley 2013	6	126	Not given
	Orji, 2002	3	84	Not given
Placental abruption	Chibber, 2015	428	728	Not given
	Luley 2013	7	126	Not given
	Orji, 2002	1	84	Not given
Preterm delivery	Chibber, 2015	97	728	Not given
Uterine rupture	Chibber, 2015	12	728	Not given
	Orji, 2002	1	84	Not given

PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	2-3
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	4
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	5
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	5
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	5-7
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	5
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	**Appendix 1**
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	5-6, **Appendix 2**
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	6-7
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	5-7
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	7
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	7-8
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	8

PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	7-8
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	7-8
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	8, **Figure 1**
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	8, **Table 1**
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	8, 9, **Figure 2**
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	9,10 **Table 2, Figure 3 Figure S1,S2 Appendix 5, 6**
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	10, **Appendix 3, 4**
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	8,9 **Figure 2**
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	9,10 **Figure S1, S2**
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	10
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	11

PRISMA 2009 Checklist

Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	12
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	3

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed1000097

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